# A PROSPECTIVE STUDY FOR DETECTING CHEMOTHERAPY RELATED CARDIAC DYSFUNCTION IN PATIENTS WITH BREAST CANCER

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I hereby declare that the thesis entitled "**A Prospective Study for Detecting Chemotherapy Related Cardiac Dysfunction in Patients With Breast Cancer''** submitted towards partial fulfillment of the requirements for the award of DM in CARDIOLOGY degree to BFUHS is a compilation of original work carried out by me under the supervision of **Dr. G S Wander**, Professor and Head, Department of Cardiology, **Dr. Bishav Mohan**, Professor, Department of Cardiology and **Dr. Davinder Paul**, Associate professor, Department of Oncology. No part of this thesis has formed the basis for the award of any degree previously.

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*Dedicated*

*to*

*my Daughter*

*Harmehar*

*Kaur*

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**Dr JASVINDER SINGH**

# ABBREVIATIONS

| | |
|---|---|
| AC | Anthracyclines |
| ACEi | Angiotensin Converting Enzyme Inhibitor |
| ASCO | American Society of Clinical Oncology |
| BMI | Body Mass Index |
| BNP | Brain Natriuretic Peptide |
| BSA | Body Surface Area |
| CAD | Coronary Artery Disease |
| CKD | Chronic Kidney Disease |
| CT | Chemotherapy |
| CTRCD | Cancer Therapeutics- Related Cardiac Dysfunction |
| DT | Deceleration Time |
| ECG | Electrocardiogram |
| ER | Estrogen Receptors |
| ESC | European Society of Cardiology |
| ESMO | European Society of Medical Oncology |
| GCS | Global Circumferential Strain |
| GLS | Global Longitudinal Myocardial Strain |
| Gy | Grey units |
| HER 3 | Human Epidermal Growth Factor Receptor 2 |
| HF | Heart Failure |
| LGE | Late Gadolinium Enhancement |
| LV D | Left Ventricular Dysfunction |
| LVEF | Left Ventricular Ejection Fraction |
| MRA | Mineralocorticoid Receptor Antagonist |
| MRI | Magnetic Resonance Imaging |
| PBCRs | Population Based Cancer Registries |
| PR | Progesterone Receptors |
| RT | Radiotherapy |
| TKIs | Tyrosine Kinase Inhibitors |
| VHD | Vulvular Heart Disease |

# ABSTRACT

**Background:** Advances in treatment of cancer have led to improved survival but have also increased morbidity due to treatment related side effects. There are very few studies available in the literature predicting the incidence of acute cardiac toxicity of chemotherapy. We prospectively evaluated incidence, time of occurrence, clinical correlates, GLS and response to HF therapy of cardio toxicity.

**Aims and Objectives:** To assess the cardiovascular complications of cancer therapy in the patients with breast cancer with special emphasis on cancer therapy related cardiac dysfunction.

**Materials And Methods:** Prospective observational study for detecting CTRCD in patients with breast cancer who came to OPD/IPD of DMCH, Ludhiana, Punjab from the period of 1$^{st}$ March 2020 to 31$^{st}$ October 2021. We assessed LVEF at baseline, at mid of chemotherapy and at end of chemotherapy. Patients developed LVD, chemotherapy was modified and started on HF therapy.

**Results:** 97 patients (50.74±10.30years) were enrolled and divided into LVD group (n=13) and no LVD group (n=84). CTRCD was developed in 13 patients (13.4%). Predictors of LV dysfunction was essential hypertension, left breast involvement, high BMI and high dose of radiotherapy although it was statistically non-significant. Higher cancer stage i.e. stage III and IV are more prone for LV dysfunction. Out of 13, 10 patients (77%) patients recovered completely and 3 (23%) patients had partial recovery. Cancer stage III-IV, Low age, low BMI, low dose of radiotherapy, low dose of mean dose of chemotherapy and Left breast involvement are markers for partial recovery.

**Conclusion:** Acute cardio toxicity is not associated with cumulative dose of anthracyclines. Early detection, modification of chemotherapy and prompt therapy of CTRCD results in substantial recovery of cardiac dysfunction.



**Keywords:** CTRCD, anthracycline, acute cardio toxicity, GLS, recovery of function

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# INTRODUCTION

Undoubtedly, advances in diagnosis and treatment of cancers have markedly improved survival rate of cancer patients. There is no exaggeration to fact that cancers are increasing at alarming rate. According to US National Cancer institute estimates that 13.7 million cancer survivors were alive in 2012, and this number will approach 18 million by 2022.[1] However, cancer therapy related adverse effects are matter of concern among physicians involved in care of cancer patients. Some cancer treatments had an adverse side effects out of which cardiovascular complication are the most important and worrisome. Thus Chemotherapy is now proved to be 'Double Edged Sword'. Cancer patients who were successfully treated with chemotherapy are suffering from cardiovascular diseases. For instance, anthracyclines, trastuzumab and some tyrosine kinase inhibitors have detrimental effect on myocardial function. In upcoming paragraphs I will shed light on prevalence of cancer, its treatment options, screening and preventive strategy for prevention of chemotherapy related cardiac dysfunction (CTRCD).

Globally, it is estimated that 19.3 million new cancer cases and almost 10.0 million cancer deaths occurred in 2020 globally. The global cancer burden is expected to further rise to 28.4 million cases in 2040, a 47% rise from 2020. Out of which Female breast cancer being the most commonly diagnosed cancer, with an estimated 2.3 million new cases (11.7%), followed by lung (11.4%), colorectal (10.0 %), prostate (7.3%), and stomach (5.6%) cancers. It is estimated that one in four of all new cases diagnosed worldwide are breast cancer. Breast cancer is the leading cause of cancer death in women (15.0%), followed by lung cancer (13.8%) and colorectal cancer (9.5%), cervical cancer ranks fourth (7.5%). [2]

In India, according to Globocon 2018, overall breast cancer is the most commonly observed cancer (14% of total cases) and is a leading cause of death (11.1%).[3] Among females, it is also most commonly

diagnosed cancer (27.7%) and a leading cause of death (23.5%). Age adjusted incidence rate of breast cancer was found as high as 41 per 100000 women from Delhi, followed by Chennai (37.9), Bangalore (34.4), and Thiruvananthapuram (33.7).[4] The number of incident cases in India are estimated to rise from 1.15 million to 1.9 million and number of deaths estimated to rise from 0.78 million to 1,33 million by 2040.[4]

While in Punjab and Chandigarh cancer incidence was found to be found comparable to other population based cancer registries (PBCRs) in India. The incidence of breast cancer in females was 4–5 times higher in the two urban registries (PBCR Chandigarh and SAS Nagar) as compared to the two rural registries (PBCR Mansa and Sangrur). The most common cancer was lung cancer among males and breast cancer among females at PBCR Chandigarh and SAS Nagar, whereas it was esophagus among males and cervical cancer among females at PBCR Mansa and breast cancer in Sangrur.[5]

From above mentioned facts it's clear now that Breast cancer is currently a major public health and economical issue because the incidence of breast cancer is increasing. Many studies showed that, due to new chemotherapy, breast cancer can be considered a curable disease. And indeed, use of a multidisciplinary approach - surgery, radiotherapy, chemotherapy - has contributed to a significant reduction in the mortality.[6] As a consequence of increased life expectancy, it becomes essential that specific oncologic therapies should be safe.

At present, anthracyclines (epirubicin, doxorubicin, daunorubicin, idarubicin) and taxanes (paclitaxel) are the two major classes of drugs for breast cancer treatment. Anthracyclines are the most commonly used and effective drugs for breast cancer treatment. Out of Anthracyclines, doxorubicin and epirubicin are commonly used in clinical practice. Cardio toxicity of Anthracycline is a prominent risk leading to morbidity and severely impacting quality of life in the patients with breast cancer.[7] The total cumulative dose of anthracyclines is the

most significant risk factor for cardiac dysfunction. Therefore it is recommended that cumulative dose of doxorubicin should not exceed 400 mg/$m^2$, and for epirubicin 900 mg/$m^2$, for daunorubicin 800 mg/$m^2$.[7] Doxorubicin is associated with a 5% incidence of congestive heart failure when the cumulative dose of 400 mg/$m^2$ is reached.[8] The most commonly accepted pathophysiological mechanism of Anthracycline induced toxicity is the oxidative stress hypothesis, which suggest that generation of reactive oxygen species and lipid peroxidation of the cell membrane damage cardiomyocytes.

Cardio toxicity of Anthracycline may be acute, early onset and or late onset. Acute toxicity develops during or within 14 days from end of treatment, which include predominately supraventricular arrhythmia, transient LV dysfunction and ECG changes develop in <1% of the patients immediately after infusion and is usually reversible. Early onset occur within one year of the treatment, while late onset manifest themselves after several years (median 7 years after treatment).[9] Further, cardio toxicity can be divided into type 1 and type 2. Type 1, is usually caused by anthracyclines by direct myocardial damage by through necrosis or apoptosis of cardiomyocytes caused by cumulative dose and is irreversible. While type 2 cardio toxicity is myocardial dysfunction rather than cell death not associated with cumulative dose and therefore usually reversible, commonly occurs with trastuzumab.[10]

A recent study by Cardinal et al involving 2625 patients (mean follow up of 5.2 years) showed 9% overall incidence of cardio toxicity after Anthracycline treatment and 98% of cases occurred within first year and were asymptomatic.[11] Risk factors for Anthracycline induced toxicity include, cumulative dose, infusion regimen, preexisting cardiac condition, hypertension, concomitant chemotherapy and age >65 years.[12]

Other conventional chemotherapies can induce myocardial dysfunction and heart failure are Cyclophosmamide, Cisplatin, Ifosamide, and Taxanes (Paclitaxel and Docetaxel). In combination with or after

Anthracycline also appear to increase the incidence of Heart failure however contribution of individual drug in multidrug regimen is difficult to assess.

Immunotherapies and targeted therapies have led to improvement in efficacy of cancer drugs. Inhibition of human epidermal growth factor receptor 2 (HER 3) signaling with either antibodies (Tratuzumab, Pertuzumab, Tratuzumab – Emtasine) have improved outcome in patients with HER2 positive breast cancer when used in conjunction with chemotherapies. Based on large scale clinical trials rate of cardiac dysfunction ranged from 7 to 34%, with heart failure rates between 0-4%. When Trastuzumab used concomitantly with Anthracyclines, rates of heart failure were 6.2% and <20.1% after one and five years respectively.[13] In patients receiving trastuzumbab, cardio toxicity is most common reason for treatment interruption in 13.5% of the patients.[14]

Radiation exposure associated with increased risk of ischemic heart disease in patients with breast cancer. Radiation to the left breast is of particular concern given its anatomical proximity to the heart, and studies have shown increased cardiovascular events in patients receiving left sided radiotherapy compared to right side. Marked interstitial myocardial fibrosis is common in radiation induced cardio toxicity.[14]

Preventive strategies of cardio toxicity involved early diagnosis, limiting cumulative dose, prolonged administration time (infusion over 24 – 96 hours), strengthening the monitoring of cardio toxicity and use of liposomal Anthracycline. Non pharmacological measures should be promoted which include healthy diet, smoking cessation, regular exercise and weight control. Prior to staring potential cardio toxic chemotherapy, risk stratification and echocardiography should be done to know the baseline Left Ventricular function. Early detection of decreased ventricular function allows modification in chemotherapy regimen, either by increasing interval between doses or reducing the

total cumulative dose of potentially toxic agent. Patients having Left ventricular dysfunction or presenting with heart failure should be treated with guidelines of heart failure.

In India there are very few studies reporting acute cardiac dysfunction in patients receiving chemotherapy for breast cancer. The present study is planned with the aim to evaluate the incidence, clinical correlates and response to therapy of cardio toxicity in Indian population.

# AIMS AND OBJECTIVES

- To evaluate baseline clinical profile and echocardiography findings in patients with breast cancer.
- To assess the cardiovascular complications of cancer therapy in the patients with breast cancer with special emphasis on cancer therapy related cardiac dysfunction.

# REVIEW OF LITERATURE

Cardio-oncology is a new field of interest in cardiology that focuses on the detection, monitoring, and treatment of cardiovascular disease occurring as a side effect of chemotherapy and radiotherapy. Advances in treatment of cancer have led to improved survival but have also increased morbidity and mortality due to treatment related side effects. Cardiovascular diseases are the most frequent and serious of these side effects which are a matter of growing concern among Cardio oncologist. Therefore it is necessary to periodically monitor cancer patients under treatment, especially those receiving anthracyclines and trastuzumab (monoclonal antibody) using mainly echocardiography or MUGA Scan.

In general, the cardiovascular complications of cancer therapy can be divided into nine main categories[14]:

1. Myocardial dysfunction and heart failure (HF);
2. Coronary artery disease (CAD);
3. Valvular disease;
4. Arrhythmias, especially those induced by QT-prolonging drugs;
5. Arterial hypertension;
6. Thromboembolic disease;
7. Peripheral vascular disease and stroke;
8. Pulmonary hypertension and
9. Pericardial complications.

There was low level of evidence supporting cardiovascular side effects of chemotherapy that has led to numerous discrepancies between cardiologist and oncologists. On account of this recently different guidelines published which include ASCO- 2019 and 2018 (American Society of Clinical Oncology), ESMO-2017 and 2020 (the European Society of Medical Oncology), and the ESC-2016 (European Society of Cardiology). All the guidelines have given detailed information regarding cardio vascular toxicities which provide more practical

approach towards diagnosis and management for physicians who take care of cancer patients.

**Pathophysiology of cardiovacular complications**

Left ventricular dysfunction and heart failure are relatively common and serious side effects. Incidence of left ventricular dysfunction vary with different chemotherapeutic agents. Out of these anthracyclines are associated with higher incidence of left ventricular dysfunction.

Table 1: Relative incidence of LV dysfunction with different chemotherapeutic agents

| Chemotherapy agents | Incidence of LV dysfunction |
|---|---|
| Anthracyclines (dose dependent) | |
| Doxorubicin (Adriamycin)<br>400 mg/$m^2$<br>550mg/$m^2$<br>700mg/$m^2$ | <br>3-5 %<br>7-26%<br>18-48% |
| Idarubicin (>90 mg/$m^2$) | 5-18% |
| Epirubicin (900mg/$m^2$) | 0.9-11.4% |
| Mitoxanthone (>120mg/$m^2$) | 2.6% |
| Liposomal anthracycline (>900mg/$m^2$) | 2% |
| Alkylating agents | |
| Cyclophosphamide | 7-28% |
| Ifosfamide<br><10 g/$m^2$<br>12.6-16 g/$m^2$ | <br>0.5%<br>17% |
| Monoclonal antibodies | |
| Trastuzumab<br>Bevacizumab<br>Petuzumab | 1.7-20.1%<br>1.6-4%<br>0.7-1.2% |

Anthracyclines

Anthracyclines have high efficacy for treatment of solid tumors like breast cancer and hematological malignancies, but their cardiac side effects have growing concern for their use. Anthracyclines may cause irreversible cardiac damage and may adversely affect the prognosis. Cardiac side effects of anthracyclines are dose dependent, for instance doxorubicin[14] is associated with 5% incidence of congestive heart failure when cumulative lifetime dose is 400mg/$m^2$ is reached, and higher dose leads to exponential increase in risk up to 48% at 700 mg/$m^2$.

Most commonly accepted pathophysiological mechanism of cardio toxicity is oxidative stress hypothesis. Anthracyclines generates reactive oxygen species and lipid peroxidation of cell membrane damage cardiomyocytes.

Cardio toxicity of anthracyclines may be acute, early and late. Acute toxicity occurs during or within 2 weeks after AC treatment which includes supraventricular arrhythmias, transient left ventricular dysfunction and ECG changes. Immediately after infusion acute toxicity usually occur in < 1% of patients. Acute toxicity are usually reversible. Early effects occur within one year of treatment while late manifest after one year. However, there is different level of risk for each patient, like patients less 5 years and patients older than 65years are at high risk. Risk factors that are associated with increased risk of cardio toxicity are given in table 2.

If anthraycline associated cardiac dysfunction detected early and treated with HF medications, patients usually have good recovery. Conversely, if detected late after onset heart failure is difficult to treat.

Table 2: Patients at high risk of for cardiovascular toxicity according to recent guidelines

| Guidelines | High risk patients |
|---|---|
| ESC - 2016 | • High dose of anthracyclines<br>• Female gender<br>• > 65 years old or <18 years old<br>• Renal failure<br>• Concomitant or previous radiotherapy involving heart<br>• Combination of chemotherapy with both type I and type II agents<br>• Established risk factors<br>• Genetic factor |
| ASC0-2017 | • High dose of anthracyclies (doxorubicin ≥250mg/$m^2$, epirubicin ≥ 600 mg/$m^2$)<br>• High dose of radiotherapy (≥30 Gy) where the heart is in the treatment field<br>• Low dose of anthracycline in comination with low dose of radiotherapy (≤30 Gy)<br>• Low dose of anthracycline(doxorubicin ≤ 250mg/$m^2$, epirubicin ≤ 600 mg/m2) or HER2 or trastuzumab alone and presence of any of the following factors:<br>1. Age ≥ 60 years<br>2. ≥2 risk factors including smoking, hypertension, diabetes mellitus, dyslipidemia, CKD and obesity.<br>3. Compromised cardiac function( LVEF 50-55%, h/o of MI, > moderate VHD) during or before CT |
| ESMO-2020 | • Prior anthracyclin based regimen<br>• > 75 years old or < 10 years<br>• Prior mediastinal or chest radiotherapy<br>• Hypertension<br>• Smoking exposure<br>• Previous combined treatment with trastuzumb and an anthracycline<br>• Elevated cardiac biomarkers before initiation of chemotherapy<br>• Baseline abnormal systolic LVEF < 50 %<br>• Preexisting Diabetes Mellitus |

Other chemotherapies that can induce myocardial dysfunction are cyclophosphamide, cisplatin, ifosfamide and taxanes. Immunotherapies

have led a substantial improvement in cancer therapy. Inhibitors of human epidermal growth factor receptor 2 with either antibodies like trasuzumab or TKIs like lapatitinb have improved outcomes in patients with HER2 positive breast cancer but concern was high risk of cardio toxicity when used with anthracyclines. Trastuzumab given either after anthracycline or using anthracycline free chemotherapy, substantially reduced the risk of cardio toxicity induced by trastuzumab.

Similarly radiotherapy is also associated with cardio toxicity. Some studies found relative risk of fatal cardiovascular events between 1 and 2.2 in patients with breast cancer. In patient with breast cancer treated in the era of 1980-2000, the risk of cardio toxicity was highest in patients with both left breast radiotherapy and chemotherapy suggesting synergistic effects.

Table 3: Anthracycline equivalence dose considering doxorubicin in rapid infusion as reference

| Drug | Relative cardiac toxicity | Incidence of HF rise > 5% when cumulative dose exceed ($mg/m^2$) |
|---|---|---|
| Doxorubicin rapid infusion | 1 | 400 |
| Epirubicin | 0.7 | 900 |
| Daunaorubicin | ~0.7 | 800 |
| Idarubicin | 0.53 | 150 |

Screening and risk stratification

First step is to identify patients at increased risk of cardio toxicity by careful assessment of cardiovascular risk factor as given in table 1. Risk assessment should include clinical history and physical examination, and baseline echocardiographic measurements. Cardiac biomarkers like BNP and troponin may be considered. There is no validated score for risk assessment. Patients who are at high risk for developing cardio toxicity should be examined by cardio oncologist.

For patients who are treated with adjuvant anthrayclines, base line cardiac function should be assessed. If patient is at high risk second assessment should be done at end of chemotherapy. Measurement of cardiac biomarkers may be considered at baseline and after each cycle. Elevation of biomarkers identifies patient at greater risk for cardio toxicity, who may benefit from measures to prevent cardio toxicity. Patients receiving high dose of cumulative total doxorubicin or equivalent dose of 240 mg/$m^2$ are at high risk of HF so baseline cardiac assessment is essential. Similarly for patients who are treated with anti-HER2 should be screened for cardio toxicity every 3 monthly and once after competition of anti HER2 therapy.

A recent study reported 9% incidence of LV impairment following anthracycline chemotherapy in 2625 patients, out of which 98% of cases reported within 12 months following last chemotherapy. Long term surveillance should be considered for those who developed cardio toxicity.

Therefore baseline assessment of LV function is recommended before starting potentially cardio toxic chemotherapy, irrespective of clinical history. For low risk patient's surveillance should be considered with echocardiography every 4 cycle of anti HER2 treatment or after 200 mg/$m^2$ of doxorubicin or equivalent dose. More frequent screening is required in high risk patients.

Table 4: Baseline evaluation, monitoring and primary prevention in patients with anthracyclines according to current guidelines

| Guidelines | Before chemotherapy | During chemotherapy | After chemotherapy |
|---|---|---|---|
| ESC - 2016 | Baseline evaluation:<br><br>1. History and clinical examination, ECG, Echo with GLS<br>2. Troponin , BNP or NT-pro BNP<br>3. CMR if echo quality is suboptimal.<br><br>Primary prevention :<br>1. Actively manage modifiable cardiovascular risk factors and diseases.<br>2. Encourage healthy diet and exercise<br>3. If HF or LVD, patient should be discussed with cardio oncologist and option of non anthracycline regimen/ or cardio protection should be considered.<br>4. If baseline risk is high or previous use of anthracycline, prophylactic cardio protective medication regimen should be considered. | Monitoring:<br><br>1. Echocardiography with GLS<br>2. For higher dose of anthraycline containing regimens and in patients with high baseline risk, earlier assessment of cardiac function after cumulative dose of doxorubicin 240mg/$m^2$ or equivalent, should be considered<br>3. Troponin may be used at each cycle of anthracycline.<br><br>Primary prevention :<br>1. Actively manage modifiable cardiovascular risk factors and diseases.<br>2. Encourage exercise and healthy dietary habits.<br>3. Dexrazoxane can be considered in adults with advanced or metastatic breast cancer who have received a cumulative dose of > 300 mg/$m^2$ doxorubicin or > 540 mg/$m^2$ of epirubicin and would benefit from continued anthracycline based therapy. | Monitoring :<br><br>1. History and clinical examination, ECG, echo with GLS at 1 and 5 years after completion of cancer treatment in survivors who have completed higher dose of anthracycline> 300 mg/$m^2$ of doxorubicin or equivalent or who developed cardio toxicityrequiring treatment.<br>2. Clinical examination, ECG, echo with GLS in elderly and in patient with high risk of cardio toxicity.<br>3. Periodic screening with cardiac imaging and biomarkers such as BNP, should be considered for survivors particularly those treated with high cumulative doses or who demonstrated reversible LVD during cancer treatment.<br><br>Primary prevention:<br>1. Actively manage modifiable cardiovascular risk factors and diseases.<br>2. Encourage exercise and healthy diet. |

| | | | |
|---|---|---|---|
| ASCO-2017 | Baseline evaluation:<br><br>1. History and Clinical examination. ECG, echo with GLS<br><br>Primary prevention:<br><br>2. Actively manage modifiable cardiovascular risk factors and disease.<br>3. Regular exercise and healthy diet. | Monitoring:<br><br>1. History and clinical examination, ECG<br>2. In patients with clinical signs or symptoms of HF the following strategy recommended:<br>• Echo with GLS, CMR or MUGA scan if echo is suboptimal<br>• Troponin , BNO, NT- pro BNP<br>• Referral to cardiologist<br>1. Routine surveillance imaging may be offered to asymptomatic patients considered to be at high risk of developing LVD<br><br>Primary prevention<br>1. Actively manage modifiable cardiovascular risk factors and disease.<br>2. Regular exercise and healthy diet.<br>3. Card protectivestrategy may be incorporated including use of dexrazoxane, continuous infusion or liposomal formulation of doxorubicin in patients planning to receive high dose anthracycline> 250 $mg/m^2$ or epirubicin> 600 $mg/m^2$ | Monitoring<br><br>1 History and clinical examination, ECG<br>2 In patients with clinical signs or symptoms of HF the following strategy recommended:<br>3 Echo with GLS, CMR or MUGA scan if echo is suboptimal<br>4 Troponin , BNO, NT- pro BNP<br>5 Referral to cardiologist<br>6 Echo with GLS may be performed b/w 6- 12 months after completion of chemotherapy in asymptomatic patients considered to be at high risk of LVD.<br>7 CMR or MUGA scan can be offered if echo not feasible<br>8 No recommendation made regarding frequency and duration of surveillance in patients at increased risk who are asymptomatic and have no evidence of LVD.<br><br>Primary prevention:<br>9 Actively manage modifiable cardiovascular risk factors and disease.<br>10 Regular exercise and healthy diet. |

| | | | |
|---|---|---|---|
| ESMO-2020 | Baseline evaluation :<br><br>1 History and Clinical examination. ECG, echo with GLS<br>2 Troponin, BNO, NT- pro BNP should be considered in high risk with preexisting significant cardiovascular diseas and those receiving high dose of anthracyclines.<br><br>Primary preventon:<br><br>3 Actively manage modifiable cardiovascular risk factors and disease.<br>4 Regular exercise and healthy diet.<br>5 In patients with LVEF < 50 % but> 40% medical therapy with ACEi or ARB/or B blockers is recommended before treatment.<br>6 In patients with normal LVEF and cardiovascular risk factors particularly those exposed to multiple cardio toxic drugs, prophylactic use of ACEi or ARB and/or b blockers may be considered. | Monitoring:<br><br>1 In patients with clinical signs or symptoms of HF, cardiology consultation with assessment of VEF and cardiac biomarkers are recommended.<br>2 In asymptomatic non metastatic patients undergoing adjuvant trastuzumabtreatment, routine surveillance consisting of cardiac imaging every 3 months should be considered.<br>3 In asymptomatic patients undergoing anti HER2 based treatment of metastaticdisease, surveillance of cv toxicity that may consist periodic physical examination, cardiac biomarkers/or cardiac imaging should be considered.<br><br>Primary prevention:<br><br>4 Actively manage modifiable cardiovascular risk factors and disease.<br>5 Regular exercise and healthy diet. | Monitoring:<br><br>1 For asymptomatic patients with normal cardiac function periodic consultation, ECG, ECHO WITH GLS should be considered at 6-12 months, at 2 years post treatment and possibly periodic thereafter.<br><br>Primary prevention<br><br>2 Actively manage modifiable cardiovascular risk factors and disease.<br>3 Regular exercise and healthy diet. |

ECG is recommended in all patients before and during treatment. It is useful to detect tachycardia, ST-T changes, conduction disturbances, QT prolongation or arrhythmias. However these changes are nonspecific.

Echocardiography is the method of choice for detecting LVD. Although 3D echocardiography is best but 2D biplane Simpson's method is recommended for estimation of LV volumes and EF. Global longitudinal myocardial strain (GLS) considered to be accurately predict subsequent LVD. According to ESC 2016 CTRDCD is defined as absolute decrease in LVEF > 10% points, to value < 50%. While subclinical LVD is defined as relative decrease in GLS of > 15% or troponin elevation from baseline and measured before and after 24 hrs of CT. As per ESMO-2020 guidelines LVD defined as absolute decrease in LVEF > 20% points or absolute decrease in > 10 % points to value < 50% or absolute decrease in LVEF to < 50%. While subclinical LVD defined as absolute decrease in GLS ≥ 5% from baseline or relative decrease in GLS ≥ 12 % or raised troponin level. ASCO - 2017 guidelines have not provided any definition of CTRCD. This decrease in LVEF can be symptomatic or asymptomatic. Although no exact interval is established, when echocardiography should be repeated during and follow up to confirm recovery. The main limitation of 2D echocardiography is reproducibility which better in 3D echo. Diastolic dysfunction is common in patients with cancer. Multigated radionuclide angiography has been used to diagnose CTRCD with good accuracy and reproducibility but its use is limited by radiation exposure and provide limited additional information on cardiac structure and hemodynamics. Cardiac MRI is use to determine cause of LVD in challenging cases. It's also useful for pericardial evaluation. LGE is useful for detecting scarring and fibrosis.

2D strain analysis was used to measure global longitudinal systolic strain from apical four, two and three chamber views. Global circumferential strain was measured from parasternal short axis view at

the level of papillary muscles. The most suitable cardiac cycle for each view was chosen. The reference point was set at the beginning of QRS complex. End systole was identified as time point in which the LV cavity was smallest. The endocardial border was traced in end systole and region of interest was adjusted to exclude pericardium by attentively aligning epicardial border. The integrity of tracking was visually confirmed in addition to automated detection in software. If necessary region of interest was readjusted. Peak systolic longitudinal strain was determined from apical views at basal, mid-ventricular and apical level in each wall and averaged into global value for each direction. Normal value of GLS vary from -15.9 to -22.1% (mean -19.7 %, 95% CI = -20.4 to 18.9%) and of GCS vary from -20.9% to -27.8% (mean -23.3%, 95% CI = -24.6 to -22.1%).[29]

In 2017, EACVI NORRE study was conducted on a total of 549 healthy subjects, which revealed lowest expected value of LV strain calculated as ±1.96 SD from mean were -16.7% in male and -17.8% in female for GLS and -22.3% and 23.6% for circumferential strain. In multivariable analysis, longitudinal strain decreased with age whereas the circumferential strain increased with age.[15]

Table 5: 2D speckle tracking echocardiographic parameters

| | Total mean ±SD | Total 95 % CI | Male mean ± SD | Male 95% CI | Female mean ±SD | Female 95% CI | P value |
|---|---|---|---|---|---|---|---|
| Longitudinal strain | | | | | | | |
| Apical 4 chamber | -22.6 ± 3 | -16.6 to 28.5 | -21.6 ± 2.8 | -16.1 to -27.1 | -23.2 ± 3 | -17.3 to -29.1 | <0.001 |
| Apical 2 chamber | -13.2 ± 3.3 | -16.8 to -29.7 | -22.4 ± 3.1 | -16.3 to -28.5 | -23.8 ± 3.3 | -17.3 to -30.3 | <0.001 |
| Apical 3 chamber | -21.6 ± 3.2 | -15.3 to 27.9 | -21.1 ± 3.1 | -15 to -27.2 | -22 ± 3.2 | -15.7 to -28.3 | 0.007 |
| Average | -22.5 ± 2.7 | -17.2 to - 27.7 | -21.7 ± 2.5 | -16.7 to - 26.7 | -23 ± 2.7 | -17.8 to -28.2 | <0.001 |
| Circumferential strain | | | | | | | |
| Basal | -29.3 ± 10.4 | -22 to -37.2 | -29.6 ± 4.1 | -21.6 to -37.6 | -29.6 ± 3.8 | -22.2 to -37 | 0.9 |
| Mid | -30.7 ± 4.6 | -21.7 to -39.7 | -30.4 ± 4.8 | -20.9 to -39.7 | -31 ± 4.4 | -22.4 to -39.6 | 0.2 |
| Apical | -36.2 ± 6.4 | -23.7 to -48.7 | -35.2 ± 6.6 | -22.3 to -48.1 | -36.9 ± 6.1 | -24.9 to -48.9 | 0.02 |
| Average | -31.9 ± 4.5 | -23.1 to -40.6 | -31.4 ± 4.6 | -22.3 to -40.5 | -32.2 ± 4.4 | -23.6 to -40.7 | 0.08 |

Cardiac biomarkers may be considered in order to detect early cardiac injury. There is no evidence to withhold treatment based on abnormal biomarkers but it indicate increased risk of cardio toxicity. Elevated troponin predicts subsequent LV dysfunction. In a small study combination of troponin with GLS might provide greatest sensitivity of 93% and negative predictive value of 91% to predict future cardio toxicity. Timing of cardio toxicity surveillance using echo and biomarkers needs to be personalized to patient context.

Patient who developed asymptomatic LVD or HF during cancer therapy likely to get benefit from ACEi or ARB and b blockers treatment.

Table 6: Diagnostic criteria and management of CT related cardiac dysfunction

| Guidelines | Diagnostic criteria | Management of CTRCD |
|---|---|---|
| ESC-2016 | CTRCD:<br>• Absolute decrease in LVEF > 10 % points to value < 50%<br><br>Subclinical LV dysfunction:<br>• Relative decrease from baseline in GLS of > 15%<br>or<br>• Troponin elevation from baseline and measured before and/or 24 hour after each chemotherapy cycle. | CTRCD<br>• ACEi or ARB in combination with beta blockers<br>• HF therapy should be continued indefinitely unless normal systolic LV dysfunction remain stale after cessation of HF therapy and no further cancer therapy is planned.<br>• In patients with Trastuzumab induced cardiac dysfunction, HF treatment can be stopped after normalization.<br><br>Subclinical left ventricular dysfunction:<br>• In patients with decrease in LVEF< 10 % points to value of > 50 % should undergo repeated assessment of LVEF shortly after and during the duration of cancer treatment.<br>• In patients with a troponin increase during treatment with high dose of athracycline, cardio protection may be considered.<br>• In patients with a GLS decreases, cancer treatment should not be stopped, interrupted or reduced. |

| | | |
|---|---|---|
| ASCO-2017 | Cardiac dysfunction :<br><br>No definition provided | Cardiac dysfunction:<br>• Referral to cardio oncologist<br>• No recommendation made regarding continuation or discontinuation of cancer therapy in individuals with LVD. This decision made by oncologist and cardiologist after full evaluation of clinical circumstances and considering risk and benefit of continuation of therapy. |
| ESMO-2020 | Anti-cancer therapy related cardiac dysfunction:<br>• Absolute decrease in LVEF of > 20% points<br>Or<br>• Absolute decrease in LVEF of > 10% points to value of < 50%<br>Or<br>• Absolute decrease in LVEF to value of < 50 %<br>Subclinical cardiac dysfunction: | Anti-cancer therapy related cardiac dysfunction:<br>• In asymptomatic patients undergoing treatment with anthracyclines, with an LVEF decrease of ≥ 40% but < 50 % , the following evaluation is recommended:<br>1. Cardio oncologist consultation<br>2. Consider initiation of cardioprotective treatment.<br>3. A statin may be considered if concomitant CAD.<br>4. Consider BNP or NT pro BNP and troponin and cardiac focused physical examination after each dose of anthracyclines.<br>5. Repeat LVEF assessment after alternate dose of anthracyclines.<br>6. If further anthracyclines based chemotherapy is planned, benefit risk assessment of continued anthracycline use well as option of non anthracycline regimen should be discussed, the use of dexrazoxane |

| | | |
|---|---|---|
| | • Absolute decrease from baseline in GLS of ≥ 5 %<br>Or<br>• Relative decrease from baseline in GLS of ≥ 12%<br>Or<br>• Troponin elevation from baseline. | and/or liposomal doxorubicin should be considered.<br>Subclinical cardiac dysfunction:<br>• In asymptomatic patients undergoing treatment with cardiotoxic anticancer therapy, with normal LVEF but a decrease in average GLS from baseline assessment (> 12% relative decrease or > 5% absolute decrease) the following evaluation/treatment should be considered:<br>1. Consider initiation of ACEi or ARB and /or BB<br>2. Repeat LVEF/GLS should be repeated with suspected cardiac toxicity.<br>3. Lifesaving chemotherapy should not be altered solely based on changes in GLS.<br>• In asymptomatic patients undergoing treatment with cardiotoxic anticancer therapy and elevation in cardiac troponin, the following should be considered:<br>1. Cardio oncologist consultation<br>2. Consider LVEF and GLS assessment with echo<br>3. Evaluate IHD<br>4. Consider cadioprotection treatment<br>5. Consider dexrazoxane<br>6. Chemotherapy may be continued without interruption if only mild elevation in cardiac biomarkers without significant LVD. |

In 2021 Prajith Jeyaprakash et al conducted meta-analysis, Cardiotoxic Effect of Modern Anthracycline Dosing on Left Ventricular Ejection Fraction: A Systematic Review and Meta-Analysis of Placebo Arms from Randomized Controlled Trials. Three databases (CENTRAL, MEDLINE, and SCOPUS) were systematically searched for randomized trials evaluating cardioprotective agents against placebo, in preventing cardiotoxicity. Echocardiography or magnetic resonance measured LVEF pre- and post-anthracycline-based chemotherapy was abstracted from placebo trial arms. The key terms included "anthracycline," "cardiotoxicity" and "randomized." A doxorubicin equivalent anthracycline dose metric was calculated to compare different anthracyclines. A random-effects model was used to pool mean difference in LVEF after anthracycline. Meta-regressions were calculated to identify variation sources. We included 660 patients from 19 trials. The weighted mean baseline LVEF across studies was 62.6%, and follow-up LVEF assessment was performed at 6 months. The pooled mean decline in LVEF among placebo arms was 5.4% (95% CI, 3.5% – 7.3%) with a doxorubicin equivalent anthracycline dose of 385 mg/m$^2$. Meta-regression analysis showed no significant difference in LVEF against doxorubicin equivalent anthracycline dose as continuous (*P*=0.29) or against published cut-offs for cardiotoxicity (250 mg/m$^2$, *P*=0.21; 360 mg/m$^2$, *P*=0.40; and 400 mg/m$^2$, *P*=0.66). The differences in mean LVEF were not associated with sex, adjunct chemotherapy, or cancer type.[16]

In 2020 Janine A M Kamphuis et al conducted a study in Netherland on Early and late anthracycline-induced cardiac dysfunction: echocardiographic characterization and response to heart failure therapy. From the population of our cardio-oncology outpatient clinic, 92 Anthracycline-induced cardiac dysfunction patients were included in this study (age 51.6 ± 16.2 years, median cumulative anthracycline dose 329 [200–329] mg/m$^2$), and a median follow-up of 25.0 [9.6–37.2] months after ACD diagnosis. Median time to ACD diagnosis for patients diagnosed early (< 1 year) and late (> 1 year) was 4.0 vs.

47.7 months respectively. There were no echocardiographic differences between patients diagnosed early vs. late (LVEF 43.6 ± 4.9% vs. 43.0 ± 6.2% and iEDV 63.6 vs. 62.9 mL/$m^2$). Eighty-three percent of patients presented with mild LV dysfunction and in 79% the LV was not dilated. Patients diagnosed early were more likely to have (partial) recovery of cardiac function upon HF treatment initiation ($p = 0.015$).[17]

In 2020, J.G.G Manaloto et al, clinical outcomes of chemotherapy induced subclinical left ventricular dysfunction among breast cancer patients detected using echocardiographic global longitudinal strain. It was a retrospective cohort study included 99 breast cancer patients who underwent anthracycline/or HER2 receptor inhibitor chemotherapy from January 1, 2016 to December 31, 2018 in a single tertiary hospital. The prevalence of subclinical LV systolic dysfunction was 18%, wherein 28% of them had subsequent overt heart failure, and 33% expired. Abnormal GLS occurred at a mean 3.5 months (range 1-8 month) after initiation of chemotherapy and at 8 months (range 6-10 months) after entire chemotherapy sessions. Development into heart failure was observed at a mean of 6.7 months (range 4-12 months) after the occurrence of abnormal GLS. Hypertension and age > 56 years were determined to be a risk factors. Abnormalities in GLS were observed at mean dose of 260mg/$m^2$ of epirubicin, lower than dose described as high risk in the literature (600mg/$m^2$ of epirubicin). In trastuzumab abnormal GLS occurred as early as 1 month after initiation. LVEF had no significant change within 2 months (p=0.56) but significantly lower within 12 months post chemotherapy (p=0.005). All-cause mortality was 3 fold higher (RR = 3.00, p=0.02) and risk of development heart failure was 4 times higher (RR = 4.74, p=0.008) in those with abnormal GLS.[18]

In 2019, Devender Kodati et al, conducted retrospective study on adverse effects of chemotherapy in breast cancer in Telengana, India. 353 patients were enrolled. During chemotherapy, some patients were given AC, T (doxorubicin, cyclophosmamide, paclitaxel) regimen and

few patients were given CAF (cyclophosmamide, doxorubicin and 5FU regimen. Among 353 patients, 344 patients shown adverse effects and 9 patients were without any adverse effects. They have identified 1,157 adverse effects in total of 344 patients, among them 16.5% were found to be cardiac effects, 60.5% were haematological effects and 22.6% were found to be in USG abdomen.[19]

In 2017 Anita Boyd, Anthracyclines induce early changes in left ventricular systolic and diastolic function: A single centre study. 140 patients were assessed by detailed echocardiography before and within seven days post treatment. LV ejection fraction (LVEF), global longitudinal strain (GLS), strain rate and radial and circumferential strain were assessed. Additionally, left atrial volumes and LV diastolic parameters were evaluated. LVEF although reduced after treatment, remained within the normal range (60±3% vs. 59±3%, p = 0.04). Triplane GLS was significantly reduced after treatment (-20.0±1.6% vs. -19.1±1.8%, p<0.001). Subclinical LV dysfunction (>11% reduction in GLS compared to before therapy) occurred in 22% (29/135). Impaired diastolic function grade significantly increased from 46% to 57% (p<0.001) after treatment. Furthermore, diastolic dysfunction was more common in the subgroup group with reduced systolic GLS compared to those without changes in GLS (30% vs. 11%; p = 0.04). No risk factors or clinical parameters were associated with the development of subclinical LV dysfunction; however the percentage change in early diastolic strain rate and the E velocity were independent predictors of >11% reduction in GLS.[20]

In 2017, a study was conducted by Mohammad Osman et al, in which they evaluated the effect of Paclitaxel on cardiac ejection fraction at Egypt. A total of 50 subjects were enrolled between 2011 to 2015 and follow up done till 30 months. During 30 months follow up 10 (20%) patients developed grade 1 (up to 5 % decrease in EF from baseline) and 2 (asymptomatic decline in EF of > 5% but < 20% from baseline) cardio toxicities. Paclitaxel cardio toxicity increased among patients with high risk features including diabetes mellitus, hypertension, prior

radiotherapy to chest wall, performance status 2 (ECOG) and age > 60 years.[21]

In 2016 Hyun Ju Yoon et al from Korea, conducted study on Chemotherapy induced left ventricular dysfunction in patients with Breast cancer. From 2003 to 2010, 712 female patients with breast cancer (55.7±10.7 years) were enrolled and divided into the LVD group (n=82, 56.7±10.1 years) and the non-LVD group (n=630, 55.6±10.8 years). Baseline clinical and treatment-related variables were compared. Chemotherapy-induced LVD developed in 82 cases (11.4%). Low body mass index (BMI), low triglyceride level, advanced cancer stage, and the use of doxorubicin, paclitaxel, trastuzumab, or radiotherapy were significant predictors of LVD in a univariate analysis. In a multivariate analysis, low BMI, advanced cancer stage, and the use of target therapy with trastuzumab were independent predictors of chemotherapy-induced LVD. Chemotherapy-induced LVD was recovered in 53 patients (64.6%), but left ventricular function was not recovered in 29 patients (35.4%).[22]

In 2015, Daniel Cardinale et al conducted a study on early detection of Anthracycline cardio toxicity and improvement with heart failure treatment at Milan, Italy. The LVEF was assessed at baseline, every 3 months during chemotherapy and for the following year, every 6 months over the following 4 years, and yearly afterward in heterogeneous cohort of 2625 patients receiving Anthracycline containing therapy. Recovery was from cardio toxicity was defined as partial (LVEF increase > 5 absolute points and > 50%) or full (LVEF increase to baseline value). The median follow was up of 5.2 years. The overall incidence of cardio toxicity was 9% (n=226). The median time elapsed between end of chemotherapy and cardio toxicity development was 3.5 months. In 98% of cases cardio toxicity occurred within first year. 11% (n=25) patients had full recovery and 71% (n=160) patients have partial recovery.[10]

In 2009, study was conducted by Anil Grover et al, on the Doxorubicin induced cardio toxicity in adult patients on chemotherapy in Mumbi, India. Study was done from January 2000 to June 2001. ECG, CXR and echocardiography was done at baseline, at 300mg/$m^2$ and at 450 mg/$m^2$ cumulative doses of Doxorubicin. 30 patients were enrolled. One (3%) patient developed congestive heart failure, while 8 (27%) patients developed subclinical cardiac dysfunction. Concomitant use of cyclophosmamide significantly increase the risk of cardiac dysfunction (P=0.048), while low BMI (<20 kg/$m^2$) and pre-existing cardiac disease showed trend towards increased risk of cardiac dysfunction (p=0.07 for both).[23]

In 2008, Marianne Ryberg et al, conducted a study on new insight into epirubicin cardiac toxicity. 1097 patients of breast cancer treated with Anthracycline were enrolled. A total of 11.4% of patients developed cardio toxicity. Risk factors for cardio toxicity included increased cumulative dose of epirubicin, patient age, and predisposition of cardiac disease, h/o mediastinal irradiation, or antihormonal treatment for metastatic disease.[24]

In 2006, P. Fumoleau et al, conducted a study on long term toxicity after adjuvant epirubicin based chemotherapy in early breast cancer (French adjuvant study group results). 3577 patients were analysed retrospectively, 2553 received epirubicin, 662 received hormonotherapy alone and 362 had no systemic treatment. After 7 year of median follow up the risk of developing a LVD after epirubicin based adjuvant chemotherapy was 1.36% and 0.21% in non epirubicin exposed group.[25]

# MATERIALS AND METHODS

**Study Design**

This was a tertiary hospital based prospective study done on Breast cancer patients from the period of 1st March 2020 to 31st October 2021 , with the aim "**FOR DETECTING CANCER THERAPY RELATED CARDIAC DYSFUNCTION IN PATIENTS WITH BREAST CANCER"** in OPD/IPD of DMCH, Ludhiana, Punjab.

**Source of data**

All newly diagnosed breast cancer patients aged more than 18 years came to Oncology wing of DMCH for chemotherapy from 1st march 2020 to 31st October 2021 were enrolled and follow up was done. Total of 108 patients were, out of 7 were excluded and 4 were lost to follow up. Data was collected for 97 patients.

**Method of collection of data**

**Inclusion Criteria:**

1. Patients who have histological proven breast cancer of any stage.
2. Age more than 18 years.

**Exclusion Criteria:**

1. Patients less than 18 years.
2. Pregnant and lactating women.
3. Past history of Valvular Heart Disease, Cardiomyopathy, CHF, Ischemic Heart Disease, symptomatic arrhythmia and Pericardial diseases.
4. Patients with advanced metastatic disease who are critically ill.

This study was approved by ethical committee of the institute and all patients were enrolled after taking informed consent. After taking written informed consent, all patients were subjected to detailed history taking with special emphasis on for risk factors of IHD such as

Diabetes Mellitus, Hypertension, Obesity, Dyslipidemia and family history of premature CAD. A detailed history and examination of cardiovascular system will be done at baseline and at each follow up. Thorough general physical examination and specific clinical examination was done including blood pressure, pulse rate. Cardiovascular examination was done to look for heart sounds, murmurs and pericardia rub. Investigations like complete blood count, Renal function test, liver function test, CXR, 12 lead ECG, 2D Echocardiography was done at baseline, at mid of chemotherapy and at end of chemotherapy.

Chemotherapy was administered in 4-6 cycles as determined by treating oncologist. Timing of first anthracycline dose as well as cumulative dose ($mg/m^2$) was calculated to equivalent doxorubincin dose.

Cardio toxicity will be defines as a decrease in LVEF > 10 percentage points from the baseline or < 50%; relative decrease from baseline in global longitudinal strain (GLS) > 15 %.[26]

Echocardiography was performed at before starting chemotherapy, mid of the chemotherapy and at the end of chemotherapy. Patients who developed LV dysfunction fourth echocardiography were done after 3 months of chemotherapy. Affected patients were managed as per heart failure guidelines. Echocardiography was performed by same physician for each patient at different times of points. M Mode, 2D echocardiography, Doppler echocardiography, tissue Doppler, GLS and GCS was measured in left lateral position and optimized images were obtained from parasternal and apical. All measurements were performed according to recommendation of American Society of Echocardiography 2020. All patients included in the study were have left ventricular ejection fraction greater than 55 % at baseline.

LV volumes were measured from apical 4 and 2 chamber views using modified Simpson’s biplane method of discs and LVEF was calculated.

Table 7: Normal values for females[27]

| Normal value for females | |
|---|---|
| Parameters | 2D SD range |
| LV internal dimension<br>Diastolic dimension (mm)<br>Systolic dimension(mm) | <br>37.8-52.2<br>21.6-34.8 |
| LV volume<br>LV EDV(ml)<br>LVESV(ml) | <br>46-106<br>14-42 |
| LV volumes normalized to BSA<br>LV EDV (ml/$m^2$)<br>LV ESV (ml/$m^2$)<br>LVEF (biplane, %)) | <br>29-61<br>8-24<br>54-74 |
| LA volume/BS(ml/$m^2$) | 16-34 |
| 2D method<br>LV mass(g)<br>LV mass/BSA( g/$m^2$) | <br>66-150<br>44-88 |
| Septal thickness (cm)<br>Posterior wall thickness (cm) | 0.6-0.9<br>0.6-0.9 |

Diastolic function were measured by trans mitral flow parameter including early E and late A diastolic filling velocity, E/A ratio and E deceleration time (DT) from apical 4 chamber with conventional pulsed wave Doppler. Pulse wave Doppler based tissue imaging was used to

measure the average peak velocity in systole (S'), peak velocity in diastole (e'), late diastole as a' and E/e' with sample volume placed at septal and lateral annulus.LV diastolic dysfunction was stratified into four grades according to ASE guidelines based on e', E/e' ratio, E/A ratio, DT as normal, impaired relaxation, pseudo normal filling or restrictive.

LA maximum volume were measured using biplane area length method from apical four and two chamber view at the end systole, just before opening of mitral valve. Then linear length is measured from center of mitral annulus to superior border of chamber in both apical four and two chamber views, shortest dimension is used. Left atrium volume is calculated by multiplying A1 with A2 diving by length, then multiplying it by 0.85, where A1 is area in one plane and A2 is the area in orthogonal plane. Once calculated, volume is then indexed with body surface area.[27]

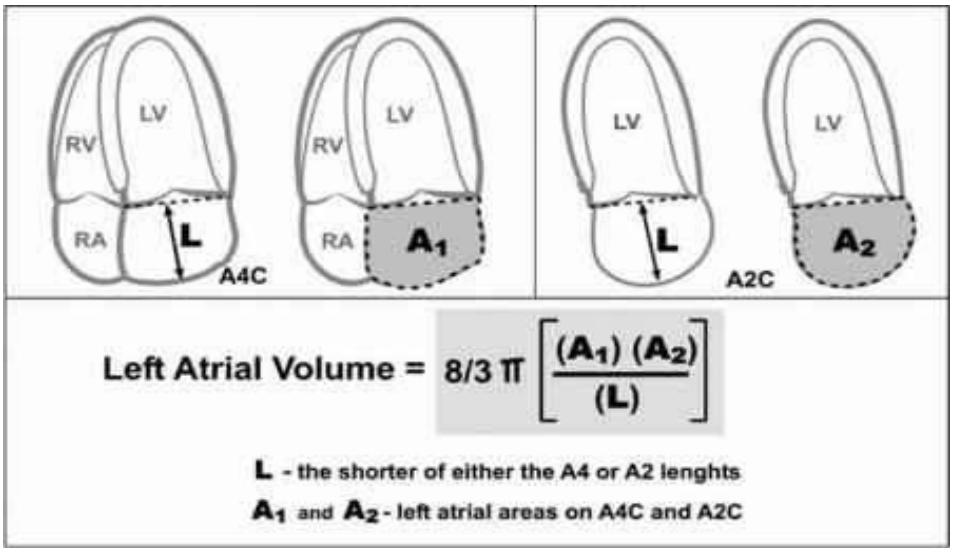



Figure 1: Left atrial volume calculation using area length method

2D strain analysis was used to measure global longitudinal systolic strain from apical four, two and three chamber views. GLS was calculated on EPIQ CVX 3D machine using software Phillip ultrasound system TMQ automated analysis for strain. Global circumferential strain was measured from parasternal short axis view at the level of

papillary muscles. The most suitable cardiac cycle for each view was chosen. The reference point was set at the beginning of QRS complex. End systole was identified as time point in which the LV cavity was smallest. The endocardial border was traced in end systole and region of interest was adjusted to exclude pericardium by attentively aligning epicardial border. The integrity of tracking was visually confirmed in addition to automated detection in software. If necessary region of interest was readjusted. Peak systolic longitudinal strain was determined from apical views at basal, mid-ventricular and apical level in each wall and averaged into global value for each direction. Normal value of GLS vary from -15.9 to -22.1% (mean -19.7%, 95% CI= -20.4 to 18.9%) and of GCS vary from -20.9% to -27.8% (mean -23.3%, 95% CI = -24.6 to -22.1%).[29]

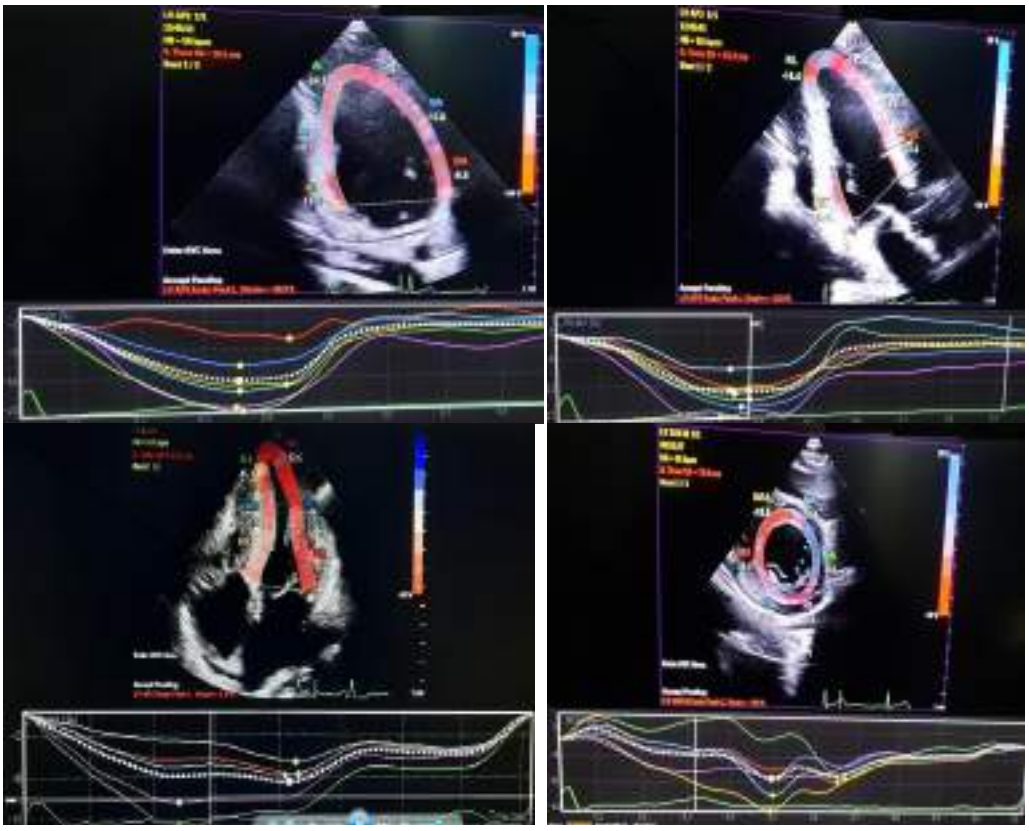


Figure 2: Echocardiography views showing GLS and GCS.

**STATISTICAL ANALYSIS:** Data were described in terms of range; mean ± standard deviation (± SD), median, frequencies (number of cases) and relative frequencies (percentages) as appropriate. Comparison of quantitative variables was done using Paired t-test. A probability value (*p* value) less than 0.05 was considered statistically significant. All statistical calculations were done using SPSS (Statistical Package for the Social Science) SPSS 21 version statistical program for Microsoft Windows.

# OBSERVATIONS AND RESULTS

This study was conducted in a tertiary care hospital on 108 female patients with histological proven diagnosis of Breast cancer. Out of which 7 patients were excluded and 4 were lost to follow up. Of the remaining 97 patients the baseline characteristics, 2D echocardiography and follow up was done. All patients were subjected to three echocardiography, first before starting chemotherapy, second at mid of the chemotherapy and third at the end of chemotherapy. Those patients who developed left ventricular dysfunction, were initiated on heart failure treatment and were follow up with fourth echocardiography after 3 months.

Table 8: Age wise distribution of Breast cancer patients

| Age group ( years) | No. of cases | Percentage |
|---|---|---|
| < 50 | 47 | 48.5% |
| 51-60 | 32 | 33.0% |
| > 60 | 18 | 18.6% |
| Total | 97 | 100.0% |

Out of total 97 female patients of breast cancer, most of the patients had age group <50 years (48.5%) where as in 51-60 years of age group there were 32 (33%) patients. Rest 18(18.6 %) of patients were in >60years age group.

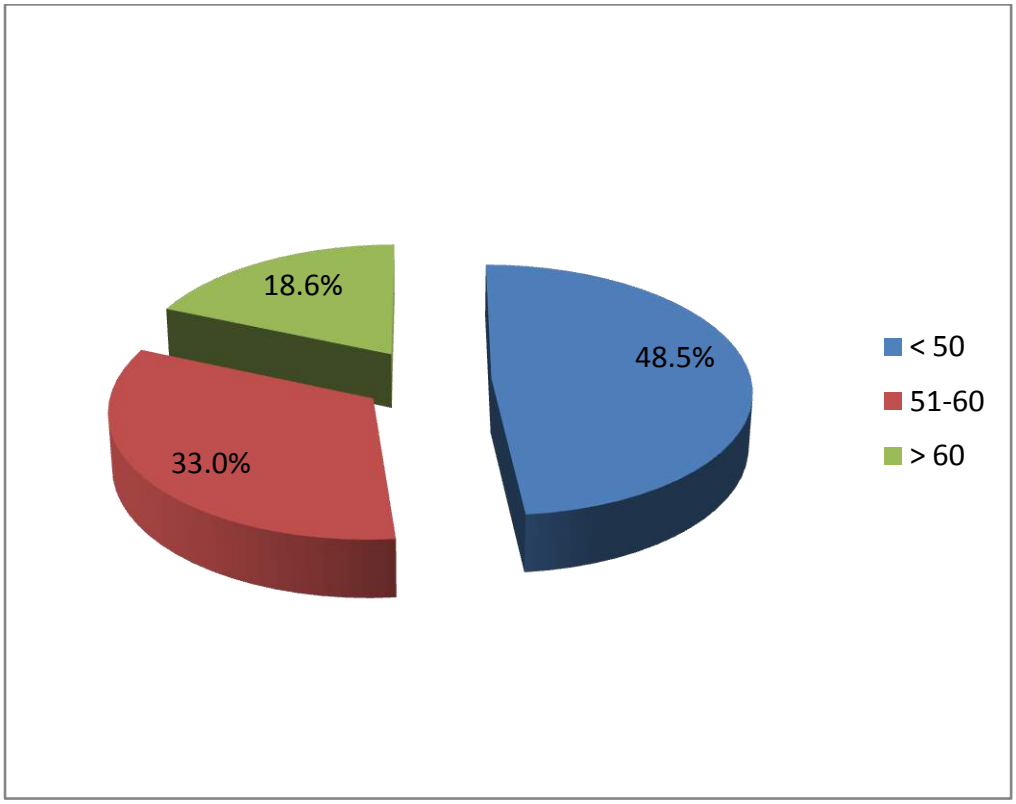



Figure 3: Age wise distribution of Breast cancer patients

Table 9: Surgical extent wise distribution of Breast cancer patients

| Surgical extent | No. of cases | Percentage |
|---|---|---|
| Left | 63 | 64.9% |
| Right | 34 | 35.1% |
| Total | 97 | 100.0% |

Out of total 97 patients of breast cancer, most of the patients had left sided involvement i.e., 63 (64.9%) patients where as in 34 (35.1%) patients right had sided involvement.

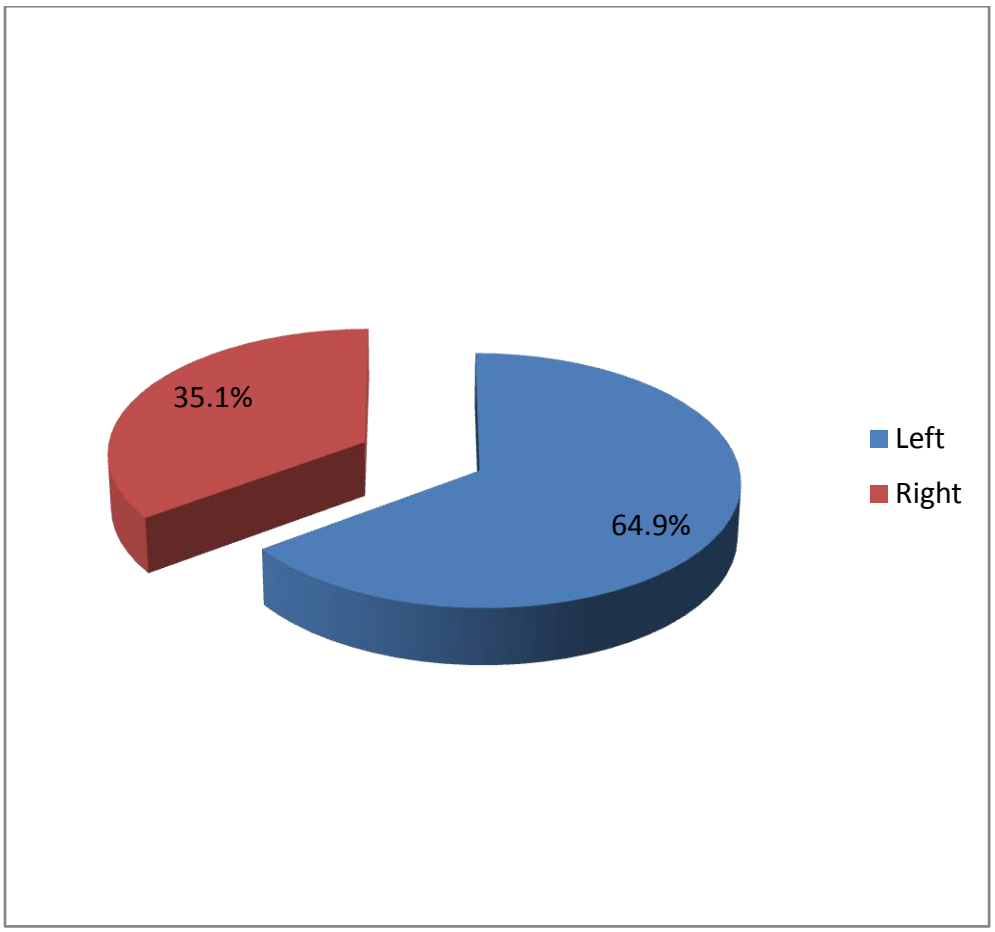



Figure 4: Surgical extent wise distribution of Breast cancer patients

Table 10: Prevalence hypertension in Breast cancer patients

| HTN | No. of cases | Percentage |
|---|---|---|
| No | 95 | 97.9% |
| yes | 2 | 2.1% |
| Total | 97 | 100.0% |

Out of total 97 patients of breast cancer, only 2 (2.1%) were hypertensive and rest 95 (97.9%) of patients were non hypertensive.

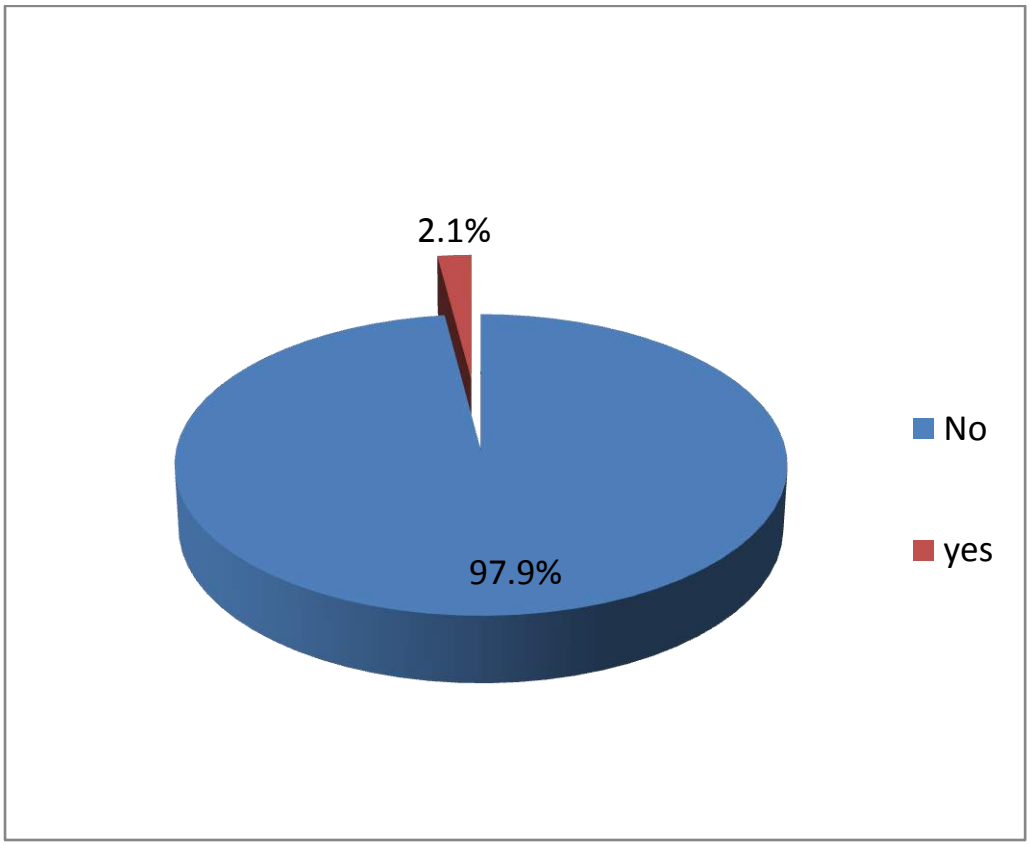



Figure 5: Prevalence hypertension in Breast cancer patients

Table 11: Prevalence Diabetes mellitus in Breast cancer patients

| DM | No. of cases | Percentage |
|---|---|---|
| No | 97 | 100.0% |
| Total | 97 | 100.0% |

Out of total 97 patients of breast cancer, none of the patients were Diabetic.

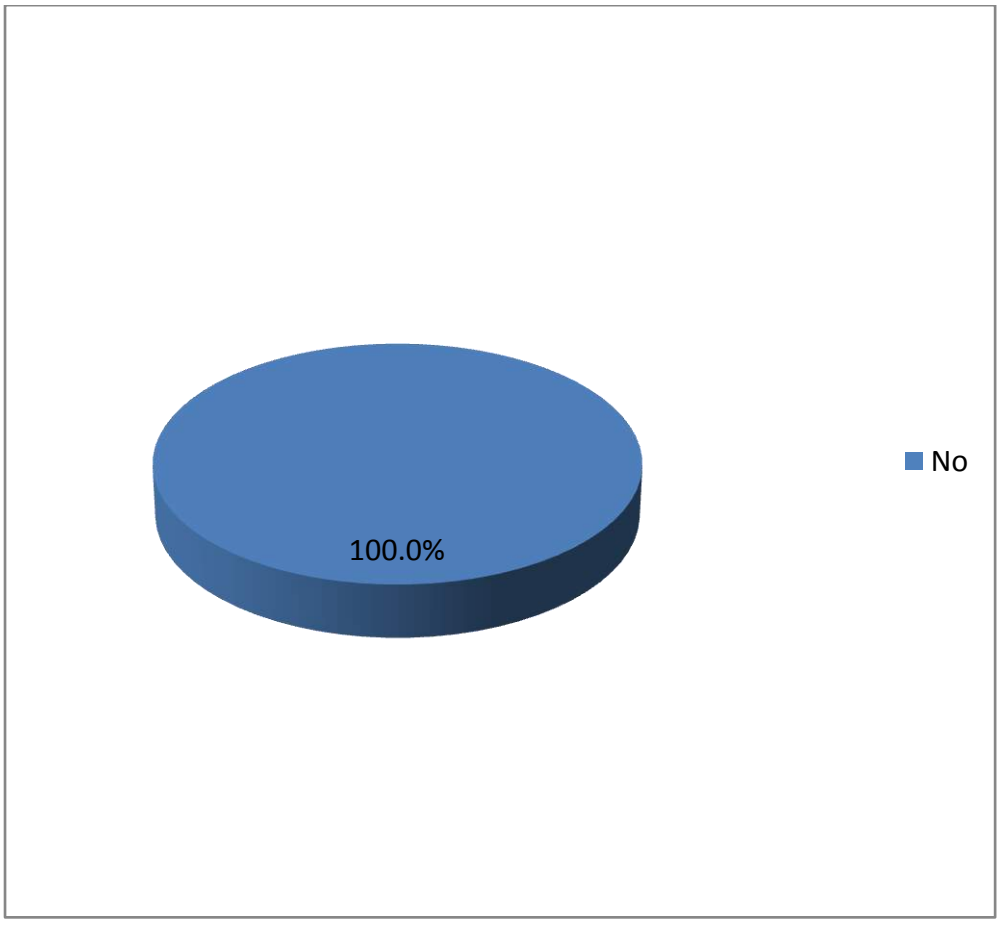



Figure 6: Prevalence Diabetes mellitus in Breast cancer patients

Table 12: Estrogen receptor wise distribution of Breast cancer patients

| ER+ | No. of cases | Percentage |
|---|---|---|
| Negative | 91 | 93.8% |
| Positive | 6 | 6.2% |
| Total | 97 | 100.0% |

Out of total 97 patients of breast cancer, 6 (6.2%) patients wereER positive and rest 91(93.8%) of patients were ER negative.

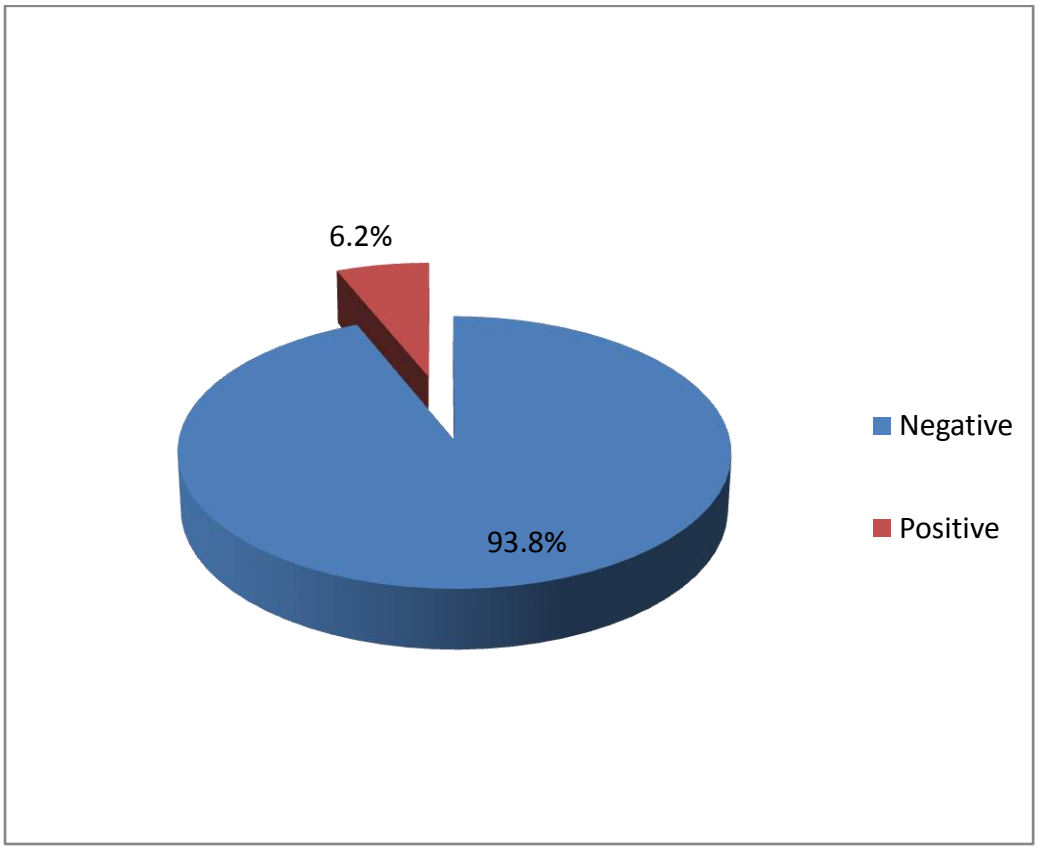



Figure 7: Estrogen receptor wise distribution of Breast cancer patients

Table 13: Progesterone receptor wise distribution of Breast cancer patients

| PR+ | No. of cases | Percentage |
|---|---|---|
| Negative | 83 | 85.6% |
| Positive | 14 | 14.4% |
| Total | 97 | 100.0% |

Out of total 97 patients of breast cancer, 14 (14.4%) patients, were PR positive and rest 83 (85.6%) of patients were PR Negative.

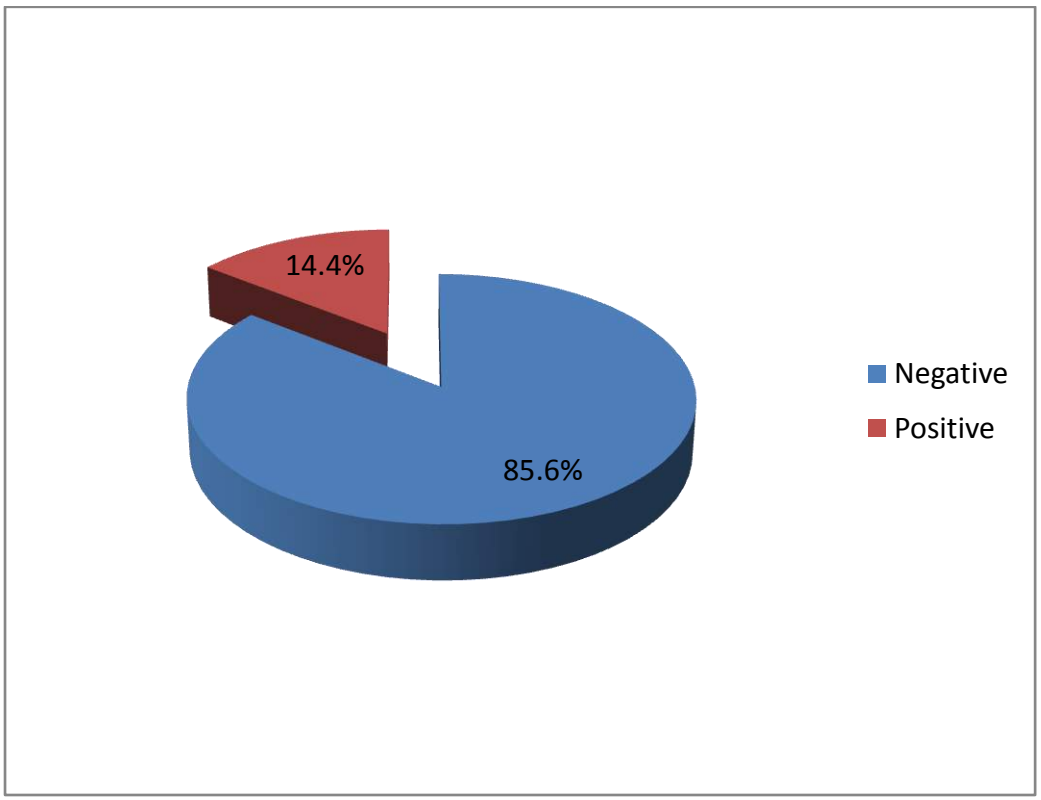



Figure 8: Progesterone receptor wise distribution of Breast cancer patients

Table 14: Human epidermal growth factor receptor 2 wise distribution of Breast cancer patients

| HER2+ | No. of cases | Percentage |
|---|---|---|
| Negative | 60 | 61.9% |
| Positive | 37 | 38.1% |
| Total | 97 | 100.0% |

Out of total 97 patients of breast cancer, 37 (38.1%) patients were Human epidermal growth factor receptor 2 positive and rest 60 (61.9%) of patients were Human epidermal growth factor receptor 2 Negative.

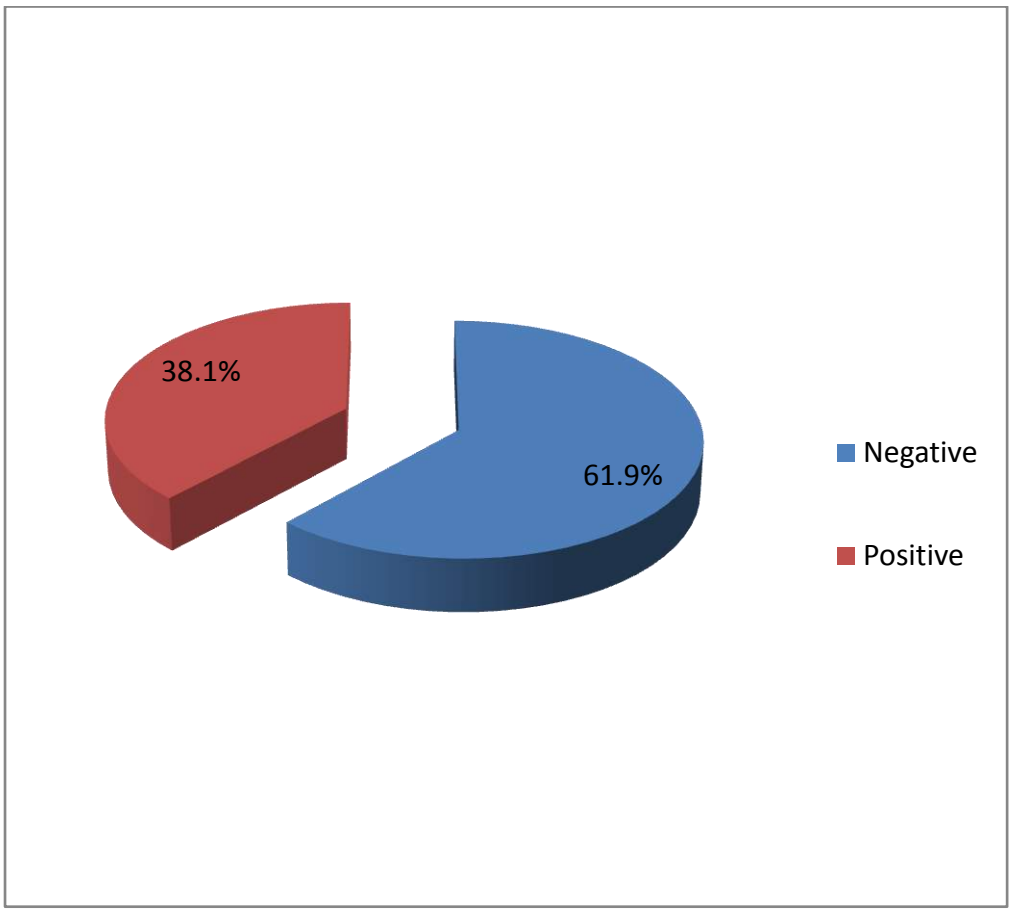



Figure 9: Human epidermal growth factor receptor 2 wise distribution of Breast cancer patients

Table 15: Cancer stage wise distribution of Breast cancer patients

| Cancer Stage | No. of cases | Percentage |
|---|---|---|
| I | 9 | 9.3% |
| II | 37 | 38.1% |
| III | 42 | 43.3% |
| IV | 6 | 6.2% |
| X | 3 | 3.1% |
| Total | 97 | 100.0% |

Out of total 97 patients of breast cancer, 42 (43.3%) patients had cancer stage III where as in 37 (38.1%) patients had stage II cancer. Cancer stage 1 was present in 9 (9.3%) patients and stage 4 present in 6(6.2 %) patients. Rest 3 (3.1%) of patients had Stage X.

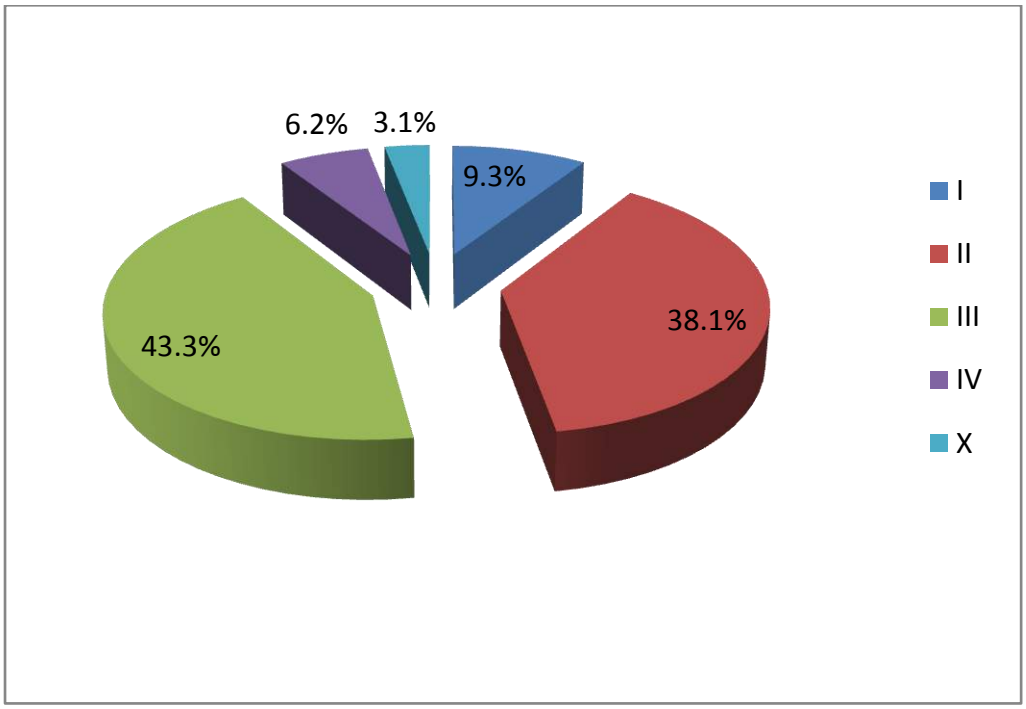



Figure 10: Cancer stage wise distribution of Breast cancer patients

Table 16: TNM staging wise distribution of Breast cancer patients

| T | No. of cases | Percentage |
|---|---|---|
| 1 | 5 | 5.2% |
| 2 | 55 | 56.7% |
| 3 | 28 | 28.9% |
| 4 | 9 | 9.3% |
| Total | 97 | 100.0% |

Out of total 97 patients of breast cancer, 55 (56.7%) patients had T2 stage where as in 28 (28.9%) patients had T2 stage.T4 stage was present in 9 (9.3%) patients and stage 1 present in 5 (5.2 %) patients.

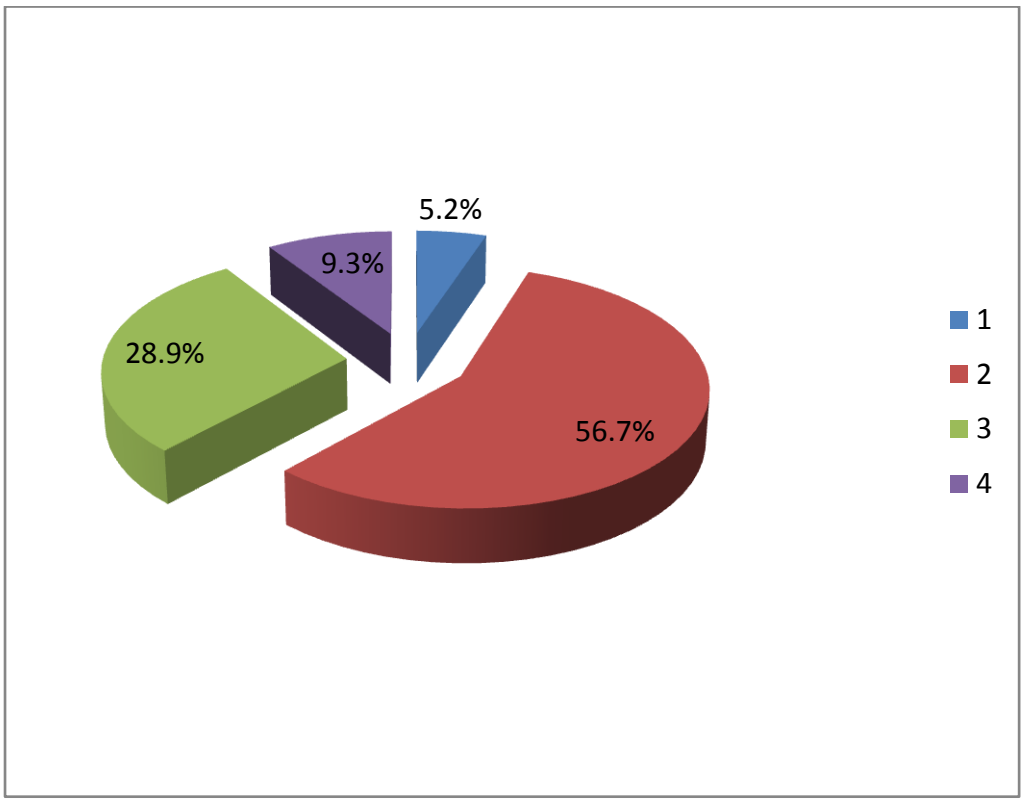



Figure 11: TNM staging wise distribution of Breast cancer patients

Table 17: TNM staging wise distribution of Breast cancer patients

| N | No. of cases | Percentage |
|---|---|---|
| 0 | 24 | 24.7% |
| 1 | 36 | 37.1% |
| 2 | 22 | 22.7% |
| 3 | 15 | 15.5% |
| Total | 97 | 100.0% |

Out of total 97 patients of breast cancer, 36 (37.1%) patients had N1 stage where as in 24 (24.7%) patients had N0 stage. N2 stage was present in 22 (22.7%) patients and stage N3 present in 15(15.5 %) patients.

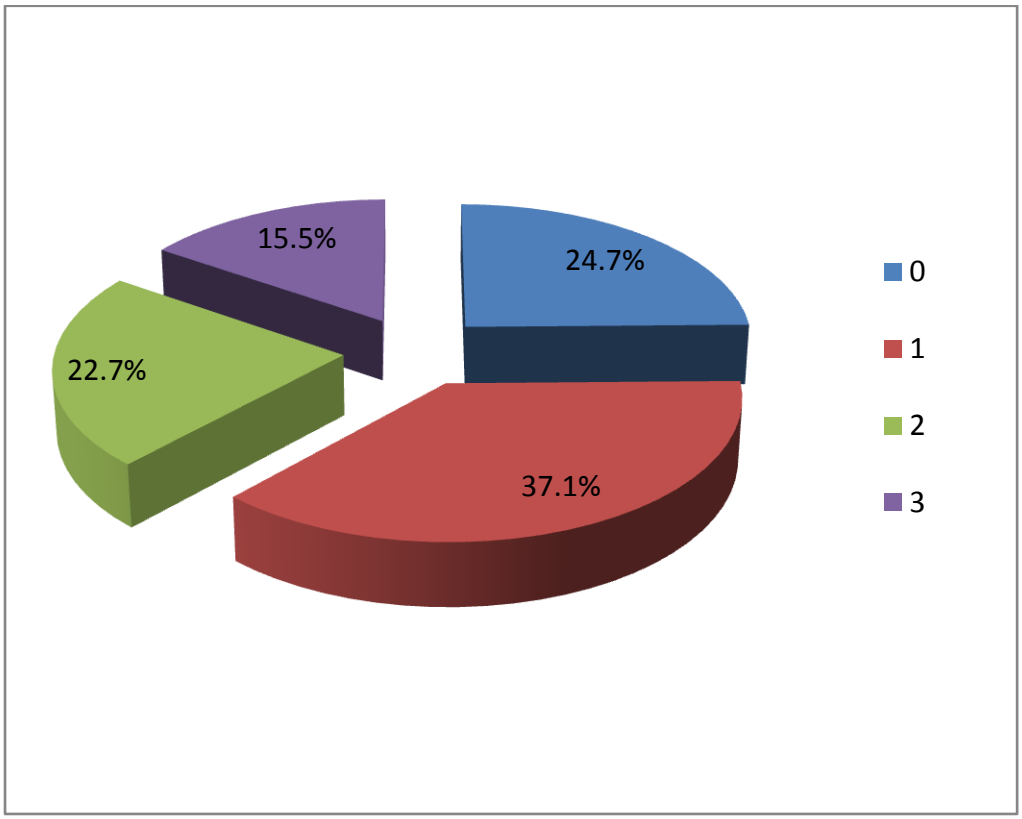



Figure 12: TNM staging wise distribution of Breast cancer patients

Table 18: TNM staging wise distribution of Breast cancer patients

| M | No. of cases | Percentage |
|---|---|---|
| 0 | 93 | 95.9% |
| 1 | 4 | 4.1% |
| Total | 97 | 100.0% |

Out of total 97 patients of breast cancer, only 4(4.1%) patients had metastatic disease M1 stage where as in 93 (95.9 %) patients had M0 stage.

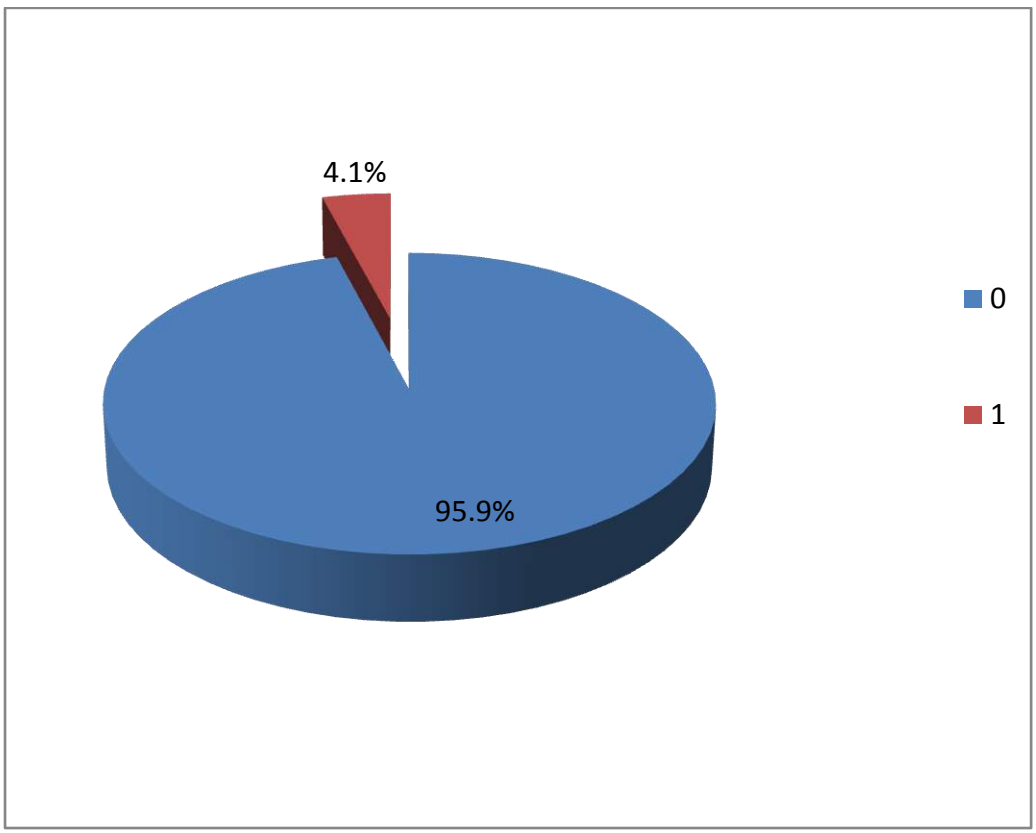



Figure 13: TNM staging wise distribution of Breast cancer patients

Table 19: Surgery wise distribution of Breast cancer patients

| Surgery | No. of cases | Percentage |
|---|---|---|
| No | 0 | 0.0% |
| Yes | 97 | 100.0% |
| Total | 97 | 100.0% |

All 97 (100%) patients of breast cancer underwent surgery before starting chemotherapy.

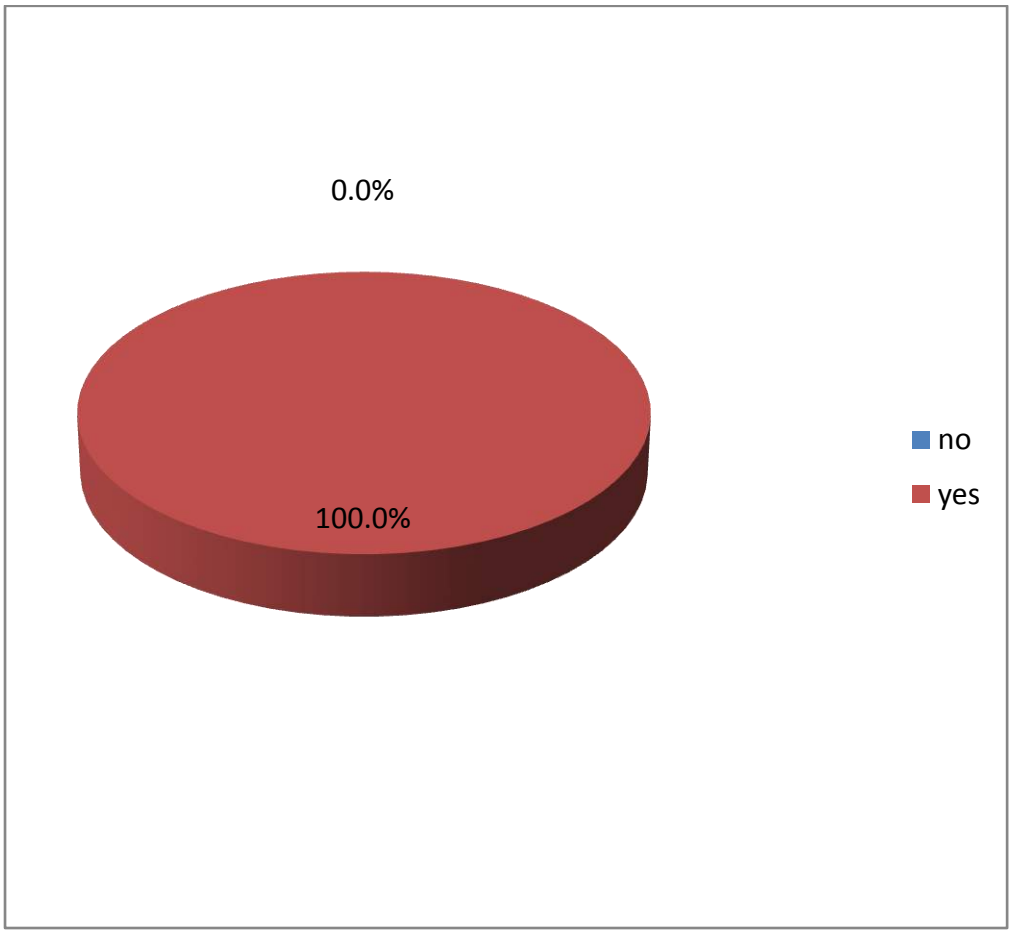



Figure 14: Surgery wise distribution of Breast cancer patients

Table 20: Radiotherapy wise distribution of Breast cancer patients

| Radiotherapy | No. of cases | Percentage |
|---|---|---|
| No | 43 | 44.3% |
| Yes | 54 | 55.6% |
| Total | 97 | 100.0% |

Out of total 97 patients of breast cancer, 54 (55.6%) patients received radiotherapy where as in 43(44.3%) didn't received radiotherapy.

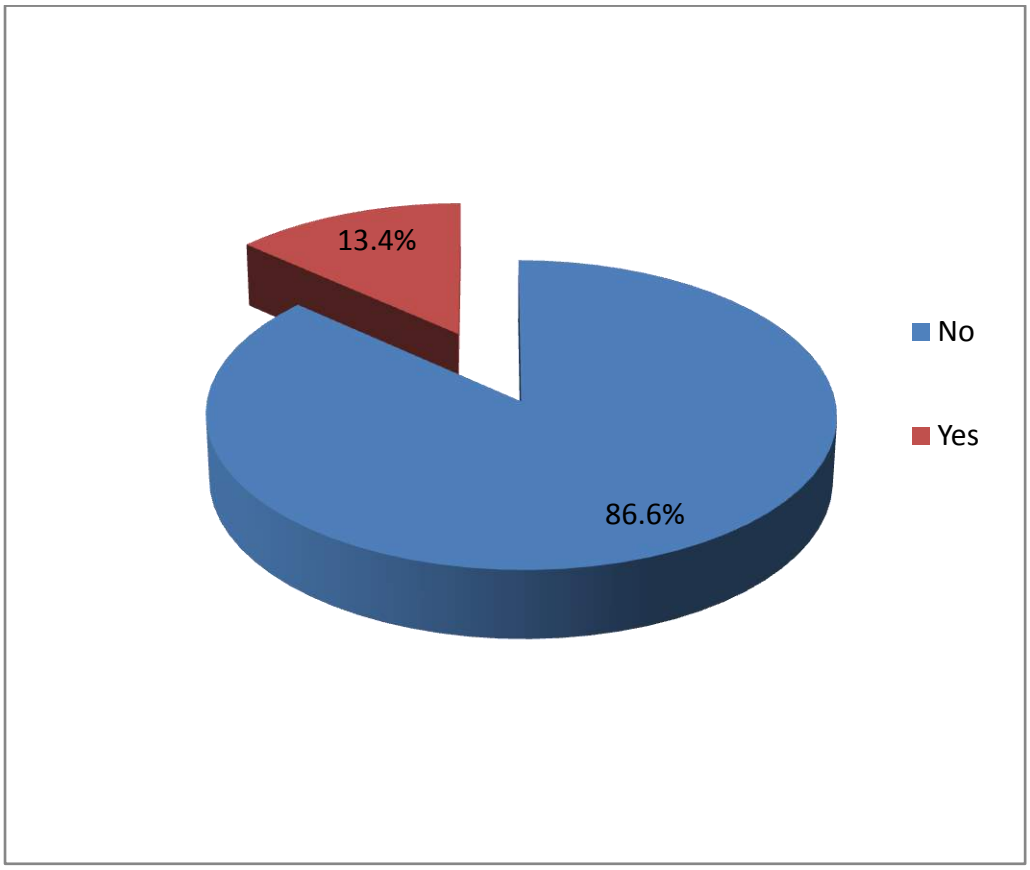



Figure 15: Radiotherapy wise distribution of Breast cancer patients

Table 21: Left ventricular dysfunction (LVD) wise distribution of Breast cancer patients

| LVD | No. of cases | Percentage |
|---|---|---|
| No | 84 | 86.6% |
| Yes | 13 | 13.4% |
| Total | 97 | 100.0% |

Out of total 97 patients of breast cancer, 13 (13.4%) patients developed LV dysfunction while 84 (86.6%) remained normal.

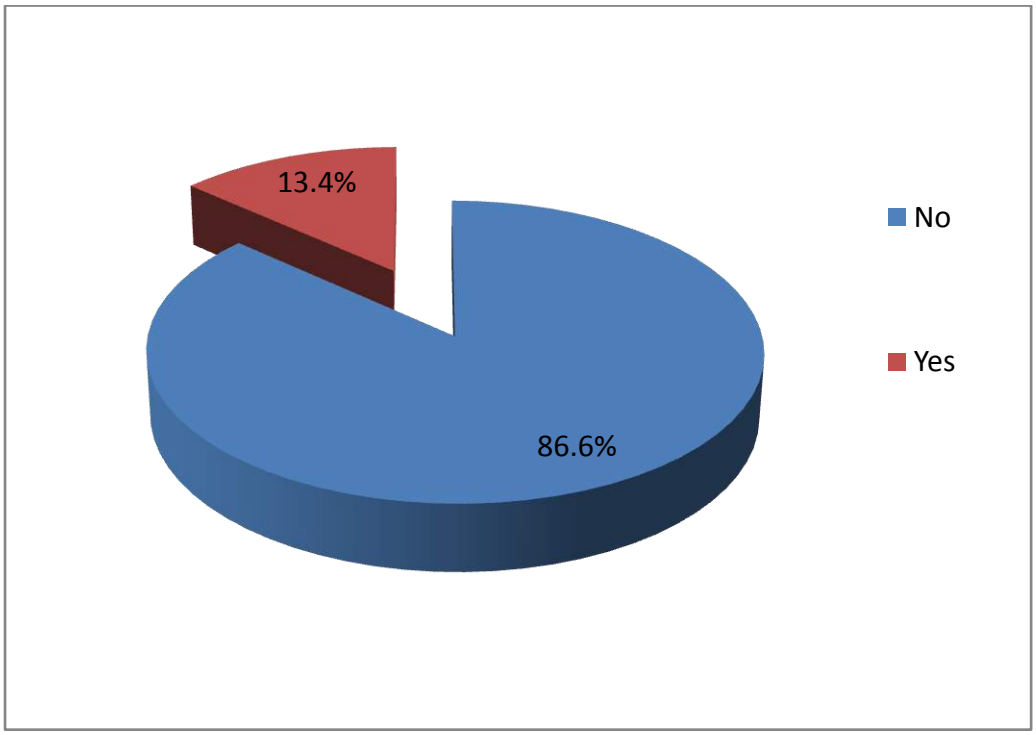



Figure 16: Left ventricular dysfunction (LVD) wise distribution of Breast cancer patients

Table 22: Age wise distribution among patients who developed LV dysfunction

| | | No LVD(n=84) | | LVD (n=13) | | Total | Chi-square value | p-value |
|---|---|---|---|---|---|---|---|---|
| Age group (years) | < 50 | 41 | 48.8% | 6 | 46.2% | 47 | 0.234 | 0.89 |
| | 51-60 | 27 | 32.1% | 5 | 38.5% | 32 | | |
| | > 60 | 16 | 19.0% | 2 | 15.4% | 18 | | |
| Total | | 84 | 100.0% | 13 | 100.0% | 97 | | |

In the present study there no significant difference between various age groups (P=0.89). Out of 97 patients 13 developed LV dysfunction. Among 13, 6 ( 46.2%) patients belong to age group of less than 50 years. 5 (38.5%) patients were from 51-60 years of age group while 2 (15.4%) patients were > 60 yrs of age.

In no LVD group, 41 (48.8%) patients belongs to age group < 50 years, 27 (32.1%) belongs to 51-60 years age group and 16 (19%) belongs to age group > 60 years.

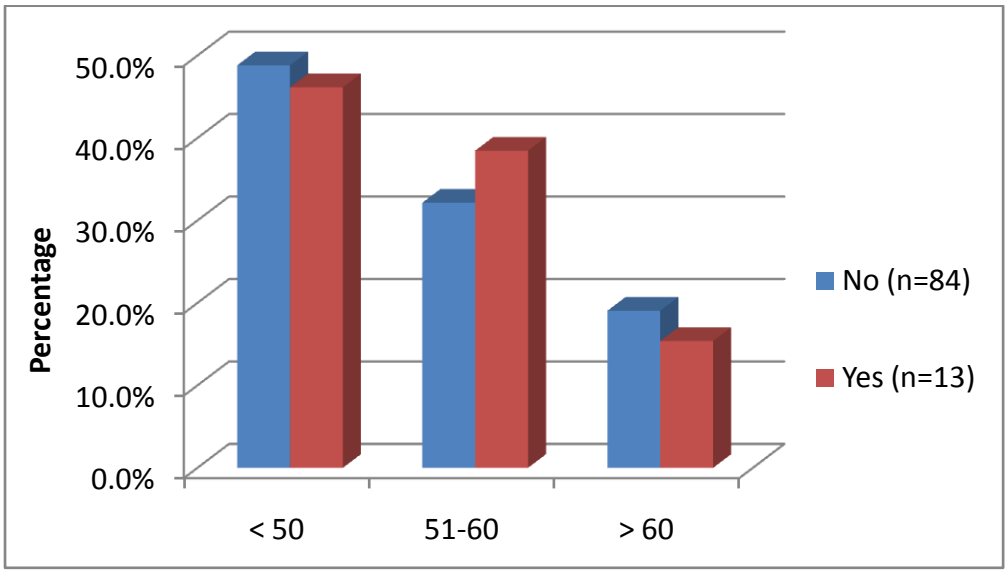



Figure 17: Age wise distribution among patients who developed LV dysfunction

Table 23: Hypertension wise distribution among patients who developed LV dysfunction

| | | No LVD (n=84) | | LVD (n=13) | | Total | Chi-square value | p-value |
|---|---|---|---|---|---|---|---|---|
| HTN | No | 84 | 100.0% | 11 | 84.6% | 95 | 13.195 | 0.017 |
| | Yes | 0 | 0.0% | 2 | 15.4% | 2 | | |
| Total | | 84 | 100.0% | 13 | 100.0% | 97 | | |

In the present study there was a significant difference between two groups in term of distribution of hypertension (P=0.017). Out of 13 patients who developed LVD, only 2 (15.4%) patients were hypertensive while 11 (15.4%) were non hypertensive. While from other 84 patients were not hypertensive. In no LVD group all 84 (100%) patients were non hypertensive.

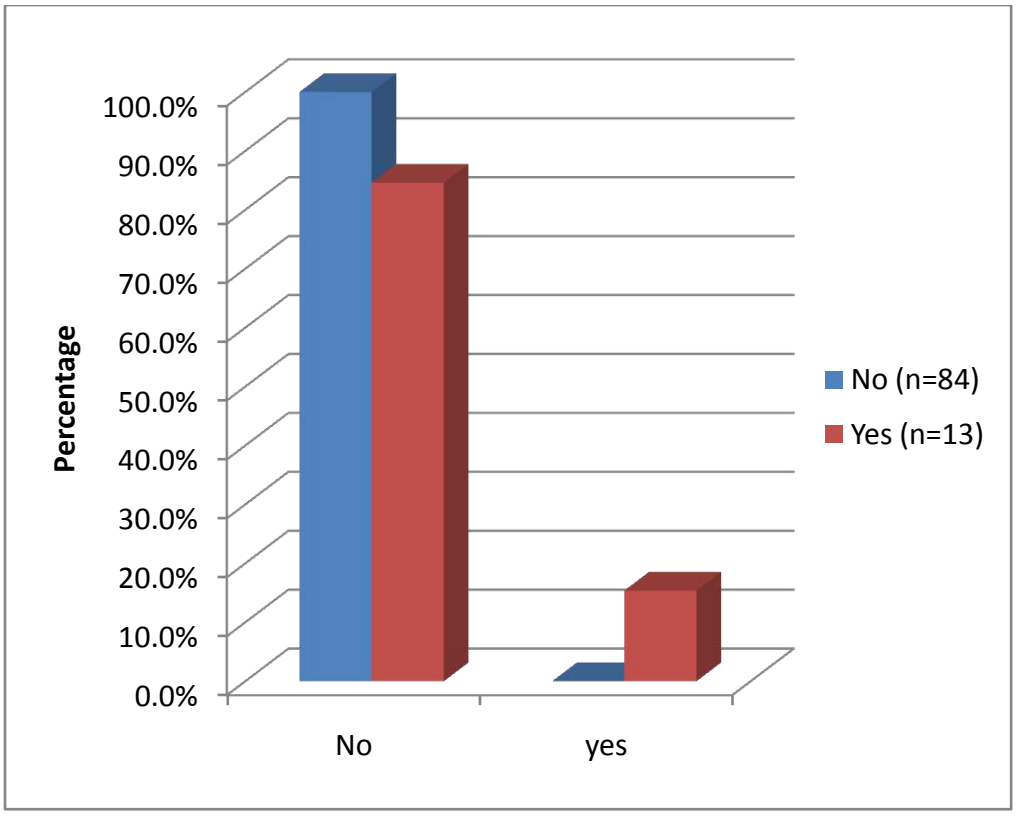



Figure 18: Hypertension wise distribution among patients who developed LV dysfunction

Table 24: Diabetes mellitus wise distribution among patients who developed LV dysfunction

| | | No LVD (n=84) | | LVD (n=13) | | Total | Chi-square value | p-value |
|---|---|---|---|---|---|---|---|---|
| DM | no | 84 | 100.0% | 13 | 100.0% | 97 | | |
| Total | | 84 | 100.0% | 13 | 100.0% | 97 | | |

No patient found to be diabetic in both the groups.

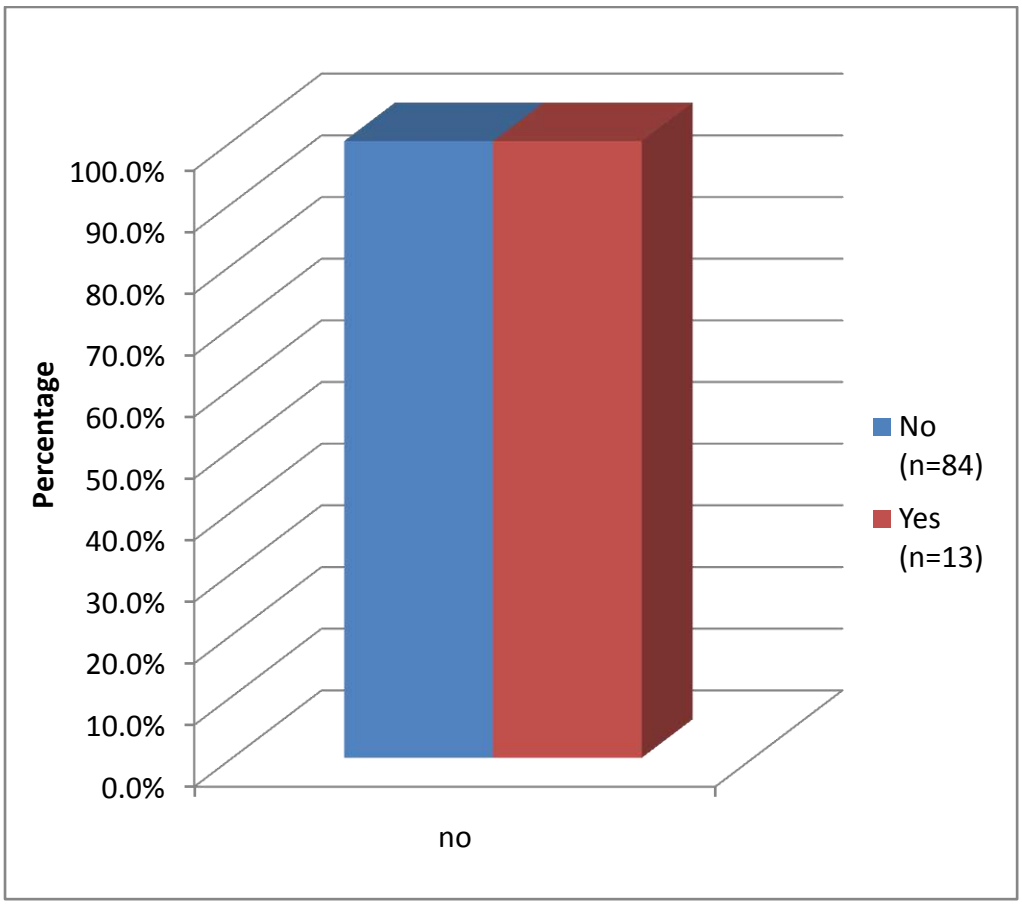



Figure 19: Diabetes mellitus wise distribution among patients who developed LV dysfunction

Table 25: Surgical extent wise distribution among patients who developed LV dysfunction

| | | No LVD (n=84) | | LVD (n=13) | | Total | Chi-square value | p-value |
|---|---|---|---|---|---|---|---|---|
| | Left | 52 | 61.9% | 11 | 84.6% | 61 | | |
| | Right | 32 | 38.1% | 2 | 15.4% | 34 | | |
| Total | | 84 | 100.0% | 13 | 100.0% | 97 | 14.676 | 0.001 |

In the present study there was a significant difference between two groups in term of distribution of surgical extent (P=0.001). Out of 13 patients who developed LVD, 11 (84.6%) patients were having left breast involved while 2 (15.4%) patients were having right breast involvement. While from other 84 patients, 52 (61.9%) were having left breast involved and 32 (38.1%) patients had right breast involved.

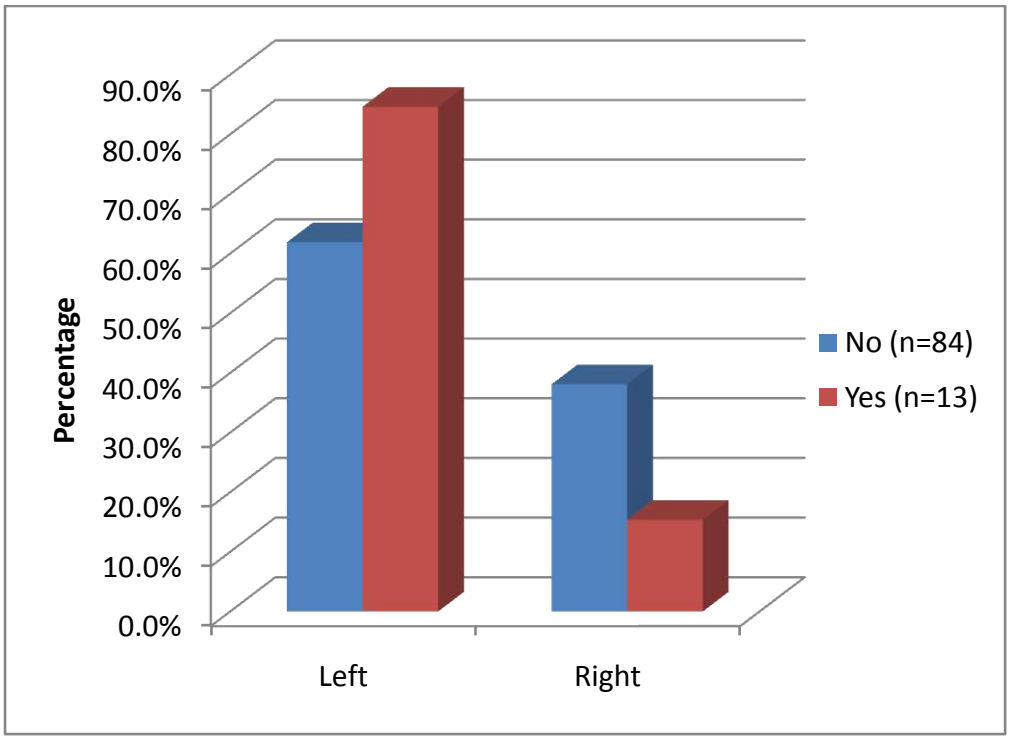



Figure 20: Surgical extent wise distribution among patients who developed LV dysfunction

Table 26: Estrogen receptor wise distribution among patients who developed LV dysfunction

| | | No LVD (n=84) | | LVD (n=13) | | Total | Chi-square value | p-value |
|---|---|---|---|---|---|---|---|---|
| ER+ | Negative | 81 | 96.4% | 10 | 76.9% | 91 | | |
| | Positive | 3 | 3.6% | 3 | 23.1% | 6 | | |
| Total | | 84 | 100.0% | 13 | 100.0% | 97 | 7.381 | 0.030 |

In the present study there was a no significant difference between two groups in term of distribution of Estrogen receptor (P=0.030).

Out of 13 patients, 10 (76.9%) patients were ER negative while 3 (23.1%) patients were ER positive. While from No LVD group 84 patients 81 (96.4%) were ER negative while 3 (3.6%) patients were ER positive.

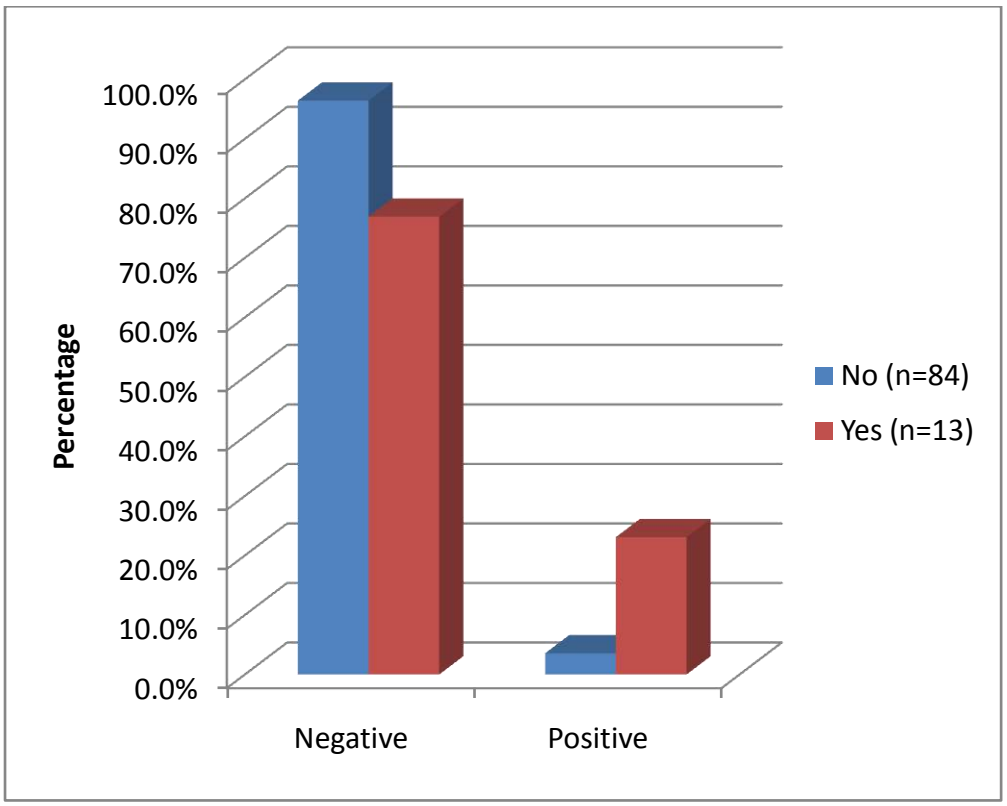



Figure 21: Estrogen receptor wise distribution among patients who developed LV dysfunction

Table 27: Progesterone receptor wise distribution among patients who developed LV dysfunction

| | | No LVD (n=84) | | LVD(n=13) | | Total | Chi-square value | p-value |
|---|---|---|---|---|---|---|---|---|
| PR+ | Negative | 73 | 86.9% | 10 | 76.9% | 83 | | |
| | Positive | 11 | 13.1% | 3 | 23.1% | 14 | | |
| Total | | 84 | 100.0% | 13 | 100.0% | 97 | 0.908 | 0.341 |

In the present study there was no significant difference between two groups in term of distribution of Progesterone receptors (P=0.341).

Out of 13 patients, 10 (76.9%) were PR negative while 3 (23.1%) patients were PR positive.

From rest of 84 patients 73 (86.9%) were PR Negative and 11 (13.1%) patients were PR positive.

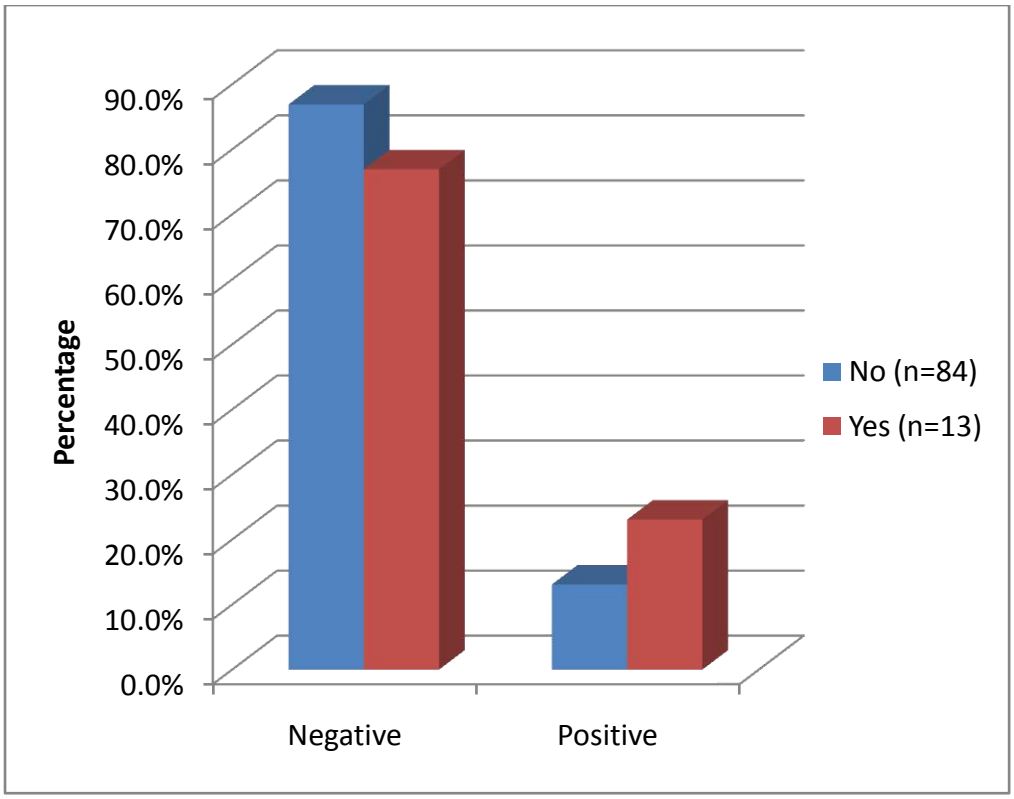



Figure 22: Progesterone receptor wise distribution among patients who developed LV dysfunction

Table 28: Human epidermal growth factor 1 receptor wise distribution among patients who developed LV dysfunction

| | | No LVD (n=84) | | LVD (n=13) | | Total | Chi-square value | p-value |
|---|---|---|---|---|---|---|---|---|
| HER2+ | Negative | 53 | 63.1% | 7 | 53.8% | 60 | | |
| | Positive | 31 | 36.9% | 6 | 46.2% | 37 | | |
| Total | | 84 | 100.0% | 13 | 100.0% | 97 | 0.408 | 0.551 |

In the present study there was no significant difference between two groups in term of distribution of HER2 (P=0.551).

Out of 13 patients, 7 (53.8%) were HER negative and 6 (46.2%) patients were HER 2 positive.

While from rest of 84 patients, 53 (63.1 %) patients were HER2 negative and 31 (36.9%) patients were HER2 positive.

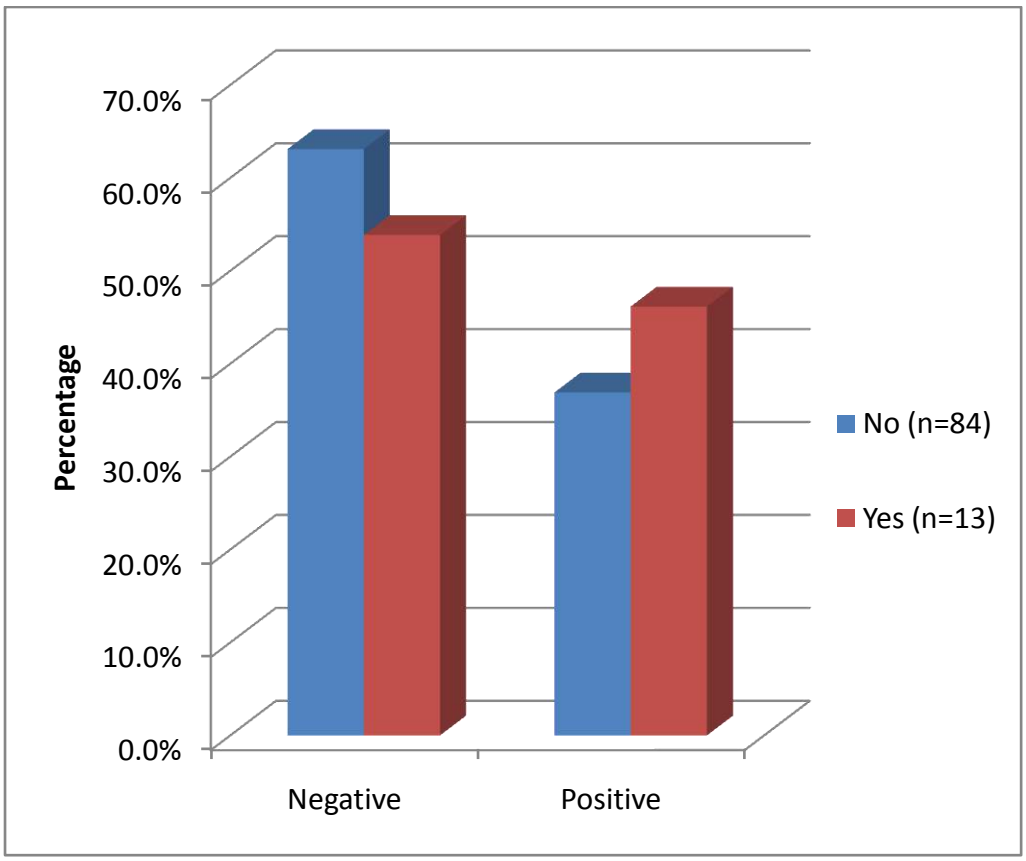



Figure 23: Human epidermal growth factor 1 receptor wise distribution among patients who developed LV dysfunction

Table 29: Cancer stage wise distribution among patients who developed LV dysfunction

| | | NoLVD (n=84) | | LVD(n=13) | | Total | Chi-square value | p-value |
|---|---|---|---|---|---|---|---|---|
| Cancer Stage | I | 9 | 10.7% | 0 | 0.0% | 9 | 4.511 | 0.341 |
| | II | 33 | 39.3% | 4 | 30.8% | 37 | | |
| | III | 35 | 41.7% | 7 | 53.8% | 42 | | |
| | IV | 4 | 4.8% | 2 | 15.4% | 6 | | |
| | X | 3 | 3.6% | 0 | 0.0% | 3 | | |
| Total | | 84 | 100.0% | 13 | 100.0% | 97 | | |

In the present study there was no significant difference between two groups in term of distribution of cancer stage (P=0.341).

Out of 13 patients, 7 (53.8%) patients were in stage III, 4 (30.8%) patients were in stage II, and 2 (15.4%) patients were in stage IV.

While in no LVD group from 84 patients, 35 (41.7%) were in stage III, 33 (39.3%) patients were in stage II, 9 (10.7%) patients were in stage 1, 4 (4.8%) patients were in stage IV and 3 (3.6%) patients were in stage X.

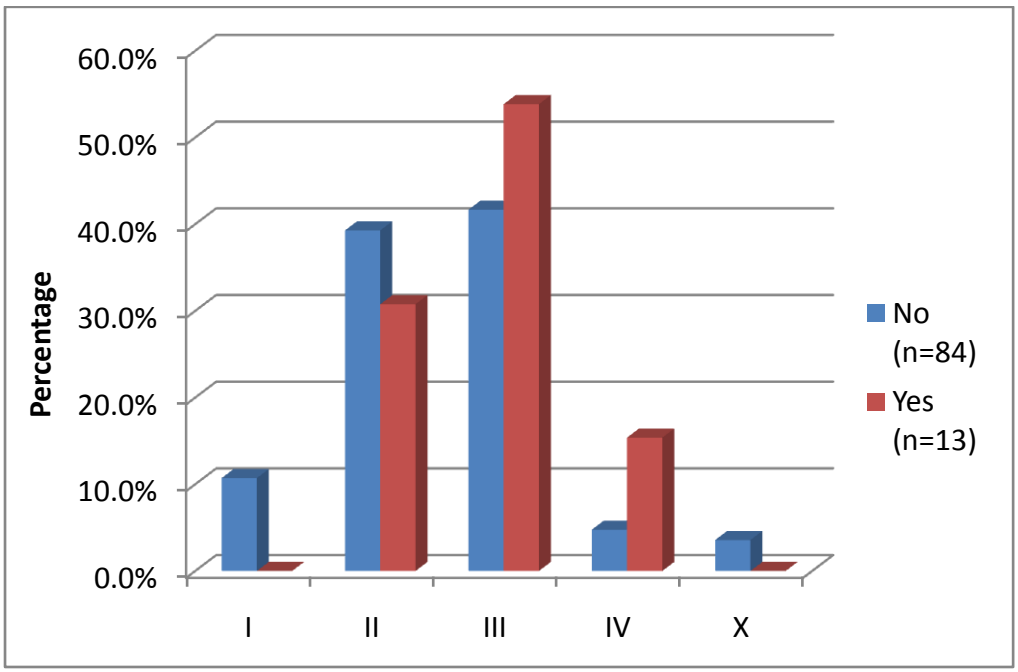



Figure 24: Cancer stage wise distribution among patients who developed LV dysfunction

Table 30: TNM stage wise distribution among patients who developed LV dysfunction

| | | No LVD (n=84) | | LVD (n=13) | | Total | Chi-square value | p-value |
|---|---|---|---|---|---|---|---|---|
| T | 1 | 3 | 3.6% | 2 | 15.4% | 5 | 7.183 | 0.066 |
| | 2 | 50 | 59.5% | 5 | 38.5% | 55 | | |
| | 3 | 25 | 29.8% | 3 | 23.1% | 28 | | |
| | 4 | 6 | 7.1% | 3 | 23.1% | 9 | | |
| Total | | 84 | 100.0% | 13 | 100.0% | 97 | | |

In the present study there was no significant difference between two groups in term of distribution of TNM staging (P=0.066).

Out of 13 patients, 5 (38.5%) patients were in T2 stage, 3 (23.1 %) patients were in each T3 and T4 stage. 2 (15.4 %) patients were in stage T1.

While in non LVD group from 84 patients 50 (59.5%) patients were in T2 stage, 25 (29.8%) were stage T3, 6 patients (7.1%) were in T4 stage and 3 (3.6%) patients were in T1 stage.

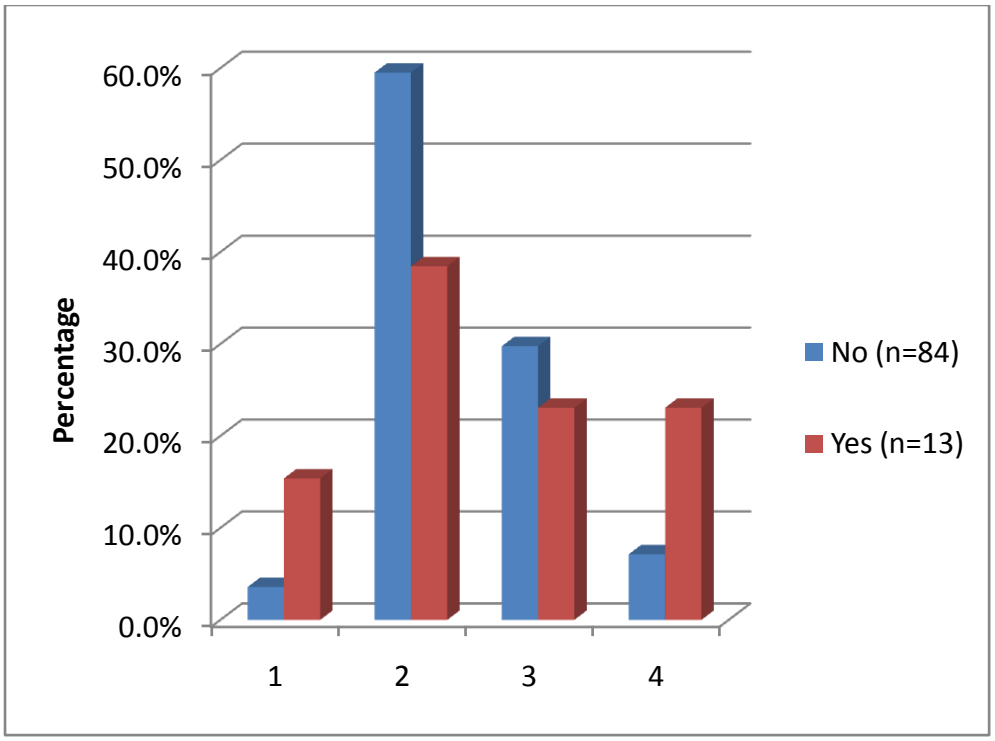



Figure 25: TNM stage wise distribution among patients who developed LV dysfunction

Table 31: TNM stage wise distribution among patients who developed LV dysfunction

| | | No LVD (n=84) | | LVD (n=13) | | Total | Chi-square value | p-value |
|---|---|---|---|---|---|---|---|---|
| N | 0 | 23 | 27.4% | 1 | 7.7% | 24 | | |
| | 1 | 30 | 35.7% | 6 | 46.2% | 36 | | |
| | 2 | 18 | 21.4% | 4 | 30.8% | 22 | | |
| | 3 | 13 | 15.5% | 2 | 15.4% | 15 | | |
| Total | | 84 | 100.0% | 13 | 100.0% | 97 | 2.527 | 0.470 |

In the present study there was no significant difference between two groups in term of distribution of TNM staging (P=0.470).

Out of 13 patients, 6 (46.2%) patients were N1 stage, 4 (30.8%) patients were in N2 stage and 2(15.4%) were in stage N3 and 1 (7.7%) patient were in stage N0.

While from 84 patients, 30 (35.7%) patients were in N1 stage, 23 (27.4%) were in N0 stage, 18 (21.4%) were in stage N2 and 13 (15.5%) patients were in N3 stage.

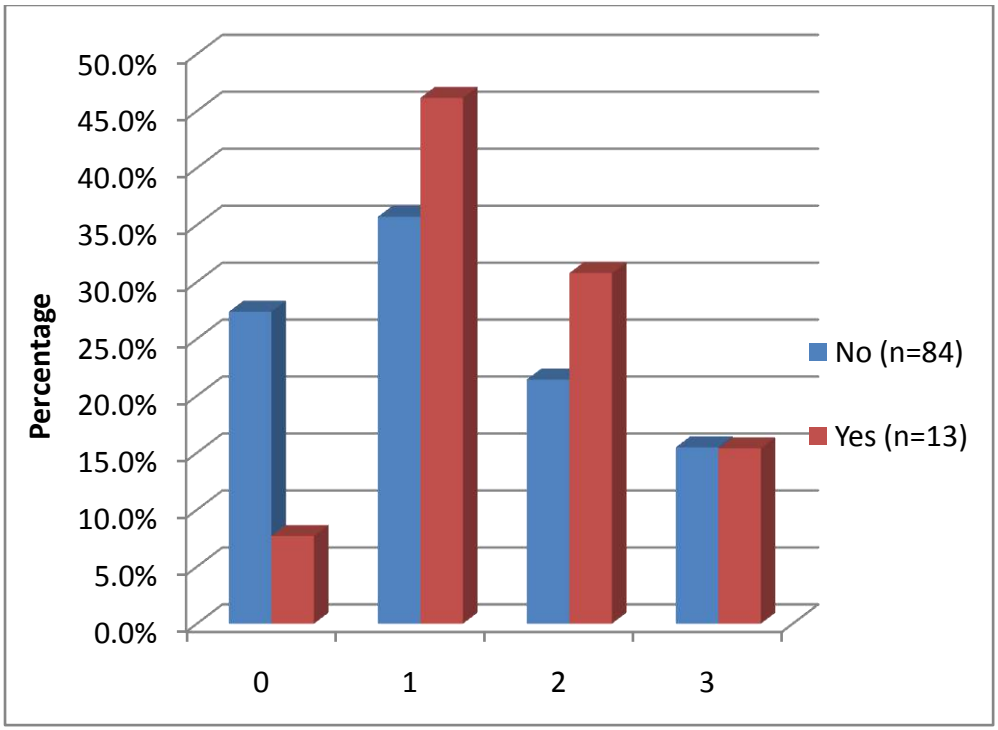



Figure 26: TNM stage wise distribution among patients who developed LV dysfunction

Table 32: TNM stage wise distribution among patients who developed LV dysfunction

| | | No LVD (n=84) | | LVD (n=13) | | Total | Chi-square value | p-value |
|---|---|---|---|---|---|---|---|---|
| M | 0 | 81 | 96.4% | 12 | 92.3% | 93 | | |
| | 1 | 3 | 3.6% | 1 | 7.7% | 4 | | |
| Total | | 84 | 100.0% | 13 | 100.0% | 97 | 0.484 | 0.487 |

In the present study there was no significant difference between two groups in term of distribution of TNM staging (P=0.487).

Out of 13 patients 1 (7.7%) patients were in M1 stage and 12 (92.3%) patients were from M0 stage.

Out of 84 patients, 81 (96.4%) patients were in M0 stage and 3 (3.6%) patients were from M1 stage.

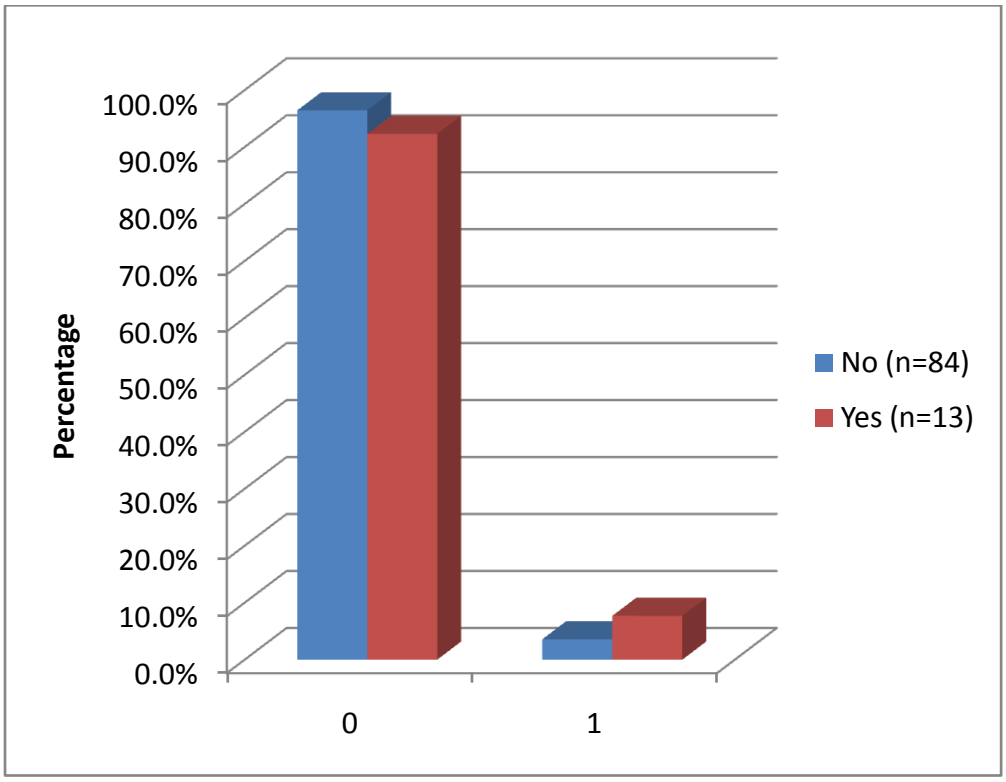



Figure 27 : TNM stage wise distribution among patients who developed LV dysfunction

Table 33: Radiotherapy and chemotherapy drugs wise distribution among patients who developed LV dysfunction

| | No LVD (n=84) | | LVD (n=13) | | Total |
|---|---|---|---|---|---|
| RT dosage Gy | 47 | 56.0% | 7 | 53.8% | 54 |
| Doxorubicin | 53 | 63.1% | 9 | 69.2% | 62 |
| Cylophosphamide | 54 | 64.3% | 10 | 76.9% | 64 |
| Trastuzumab | 31 | 36.9% | 5 | 38.5% | 36 |
| Carboplatin | 27 | 32.1% | 5 | 38.5% | 32 |
| Paclitaxel | 27 | 32.1% | 6 | 46.2% | 33 |
| Docetaxel | 0 | 0.0% | 4 | 30.8% | 4 |

Total 54 patients out of 97 received Radiotherapy.

Out of 13 patients who developed LVD, 7 (53.8%) patients received radiotherapy.

Out of 84 patients in no LVD group, 47 (56%) patients received radiotherapy.

Out of 97, one drug was received by 6 (6.1%) patients; two drugs were received by 58 (59.7%) patients, three drugs by 21 (21.6) patients and four drugs combination by 12 (12.37%) patients. Doxorubicin was prescribed to 62 patients.

Out of 13, 9 (69.2%) patients developed LVD and 53 out of 84 (63.1%) remained normal. Similarly, Cyclophosphamide was prescribed to total 64 patients out of 97. 10 patients out of 13 (76.9%) patients developed LVD. While 54 out of 84(64.3%) patients remained normal. Trastuzumab was given to 36 patients. Out of 13, 5 (38.5%) patients developed LVD and 31 (36.9%) patients remained normal. Carboplatin was given to 32 patients, 5 (38.5 %) patients developed LVD while 27 (32.1%) remained normal. Paclitaxel was prescribed to 33 patients. 6 out of 13 (46.2%) patients developed LVD. 27 (32.1 %) patients remained normal. Decetaxel was given only to LVD group, 4 out 13 (30.8%) patients received Docetaxel.

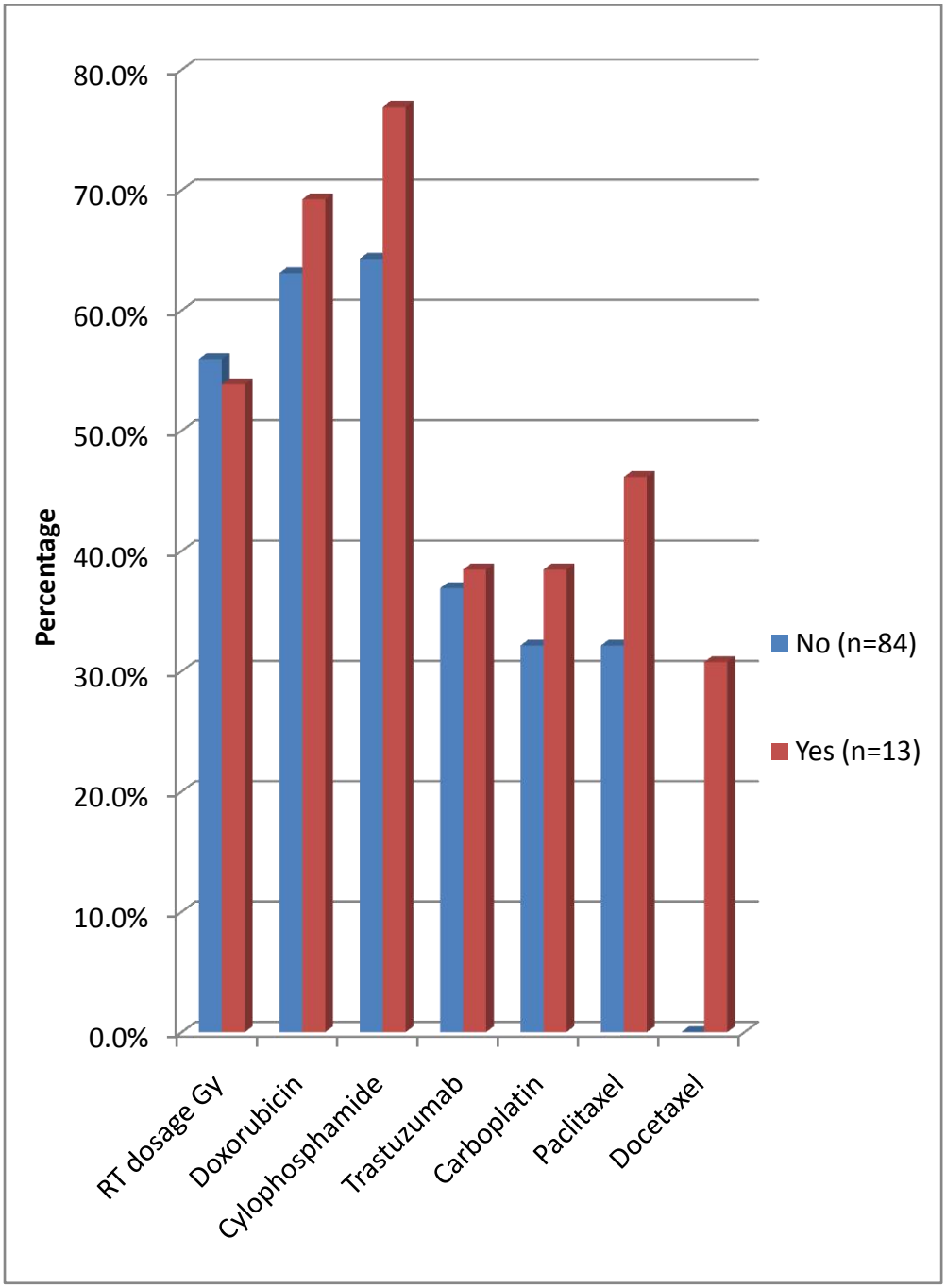



Figure 28: Radiotherapy and chemotherapy drugs wise distribution among patients who developed LV dysfunction

Table 34: Mean age wise distribution among patients who developed LV dysfunction

| | No LVD (n=84) | | LVD (n=13) | | t/Z | p-value |
|---|---|---|---|---|---|---|
| | Mean | SD | Mean | SD | | |
| Age | 50.77 | 10.62 | 50.54 | 8.30 | -0.133 | 0.895 |

In the present study there was no significant difference between two groups in term of mean distribution of age (P=0.895).

Mean age in LVD group was 50.4 and 50.77 in non LVD.

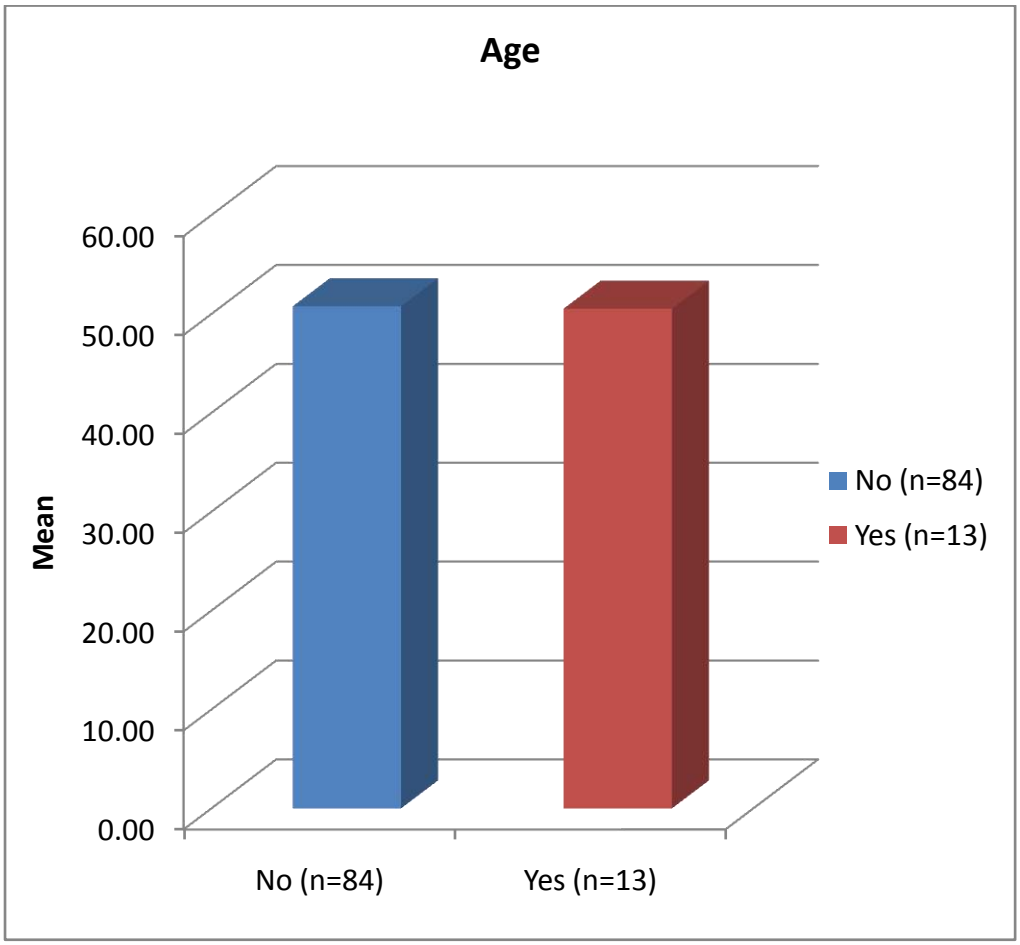



Figure 29: Mean age wise among patients who developed LV dysfunction

Table 35: Mean haemoglobin, albumin, BSA and BMI wise among patients who developed LV dysfunction

| | No LVD (n=84) | | LVd (n=13) | | t/Z | p-value |
|---|---|---|---|---|---|---|
| | Mean | SD | Mean | SD | | |
| Haemoglobin | 10.53 | 1.65 | 10.88 | 1.11 | -0.747 | 0.457 |
| Albumin | 3.97 | 0.44 | 3.94 | 0.34 | 0.302 | 0.764 |
| BMI | 27.60 | 4.36 | 29.72 | 6.60 | -1.511 | 0.134 |
| BSA | 1.67 | 0.10 | 1.64 | 0.14 | 0.797 | 0.374 |

In the present study there was no significant difference between two groups in term of distribution of Haemoglobin (P=0.457), Albumin (P=0.764), BMI (P=0.134) and BSA (P=0.374).

Mean haemoglobin was 10.88 in LVD group while it was 10.53 in no LVD group. Similarly, albumin was 3.94 in LVD group while 3.97 in no LVD group.

Body mass index was higher in i.e. 29.72 in LVD group while 27.60 in no LVD group.

Body Surface area was1.64 in LVD group while 1.67 in no LVD group.

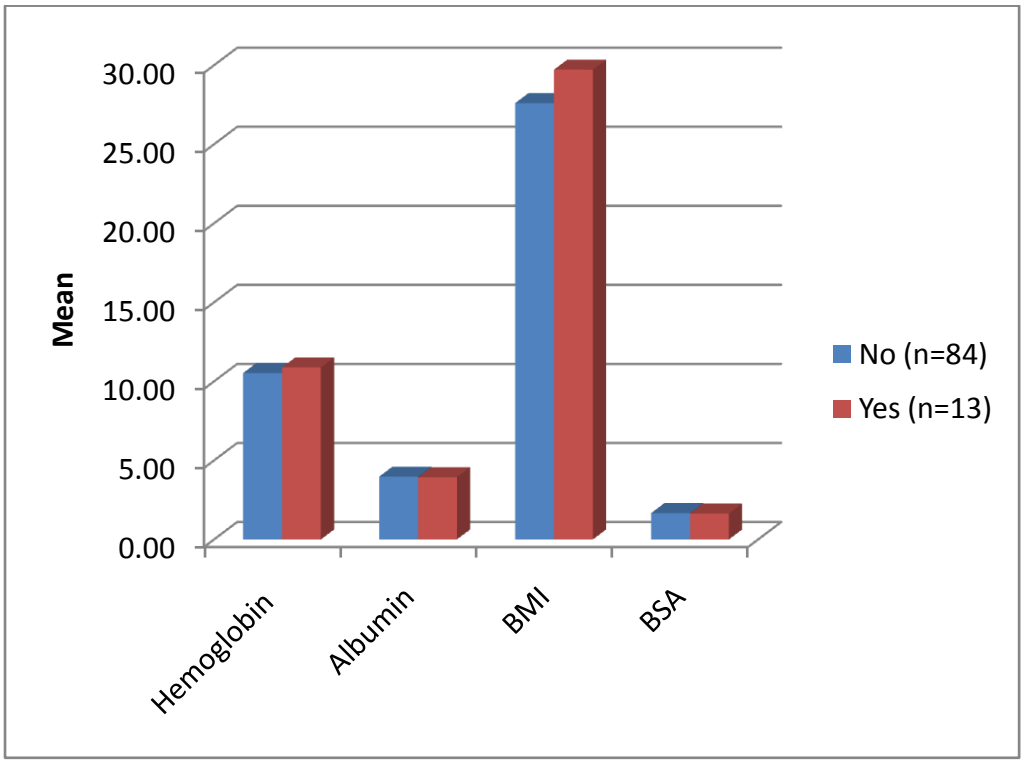



Figure 30: Mean haemoglobin, albumin, BSA and BMI wise among patients who developed LV dysfunction

Table 36: Mean radiotherapy wise among patients who developed LV dysfunction

| | No LVD (n=84) | | LVD (n=13) | | t/Z | p-value |
|---|---|---|---|---|---|---|
| | Mean | SD | Mean | SD | | |
| RT dosage Gy | 44.32 | 7.43 | 48.97 | 4.02 | -1.615 | 0.112 |

In the present study there was no significant difference between two groups in term of distribution of radiotherapy (P=0.112).

Mean radiotherapy dose was higher i.e. 48.97 in LVD group while it was 44.32 in no LVD group.

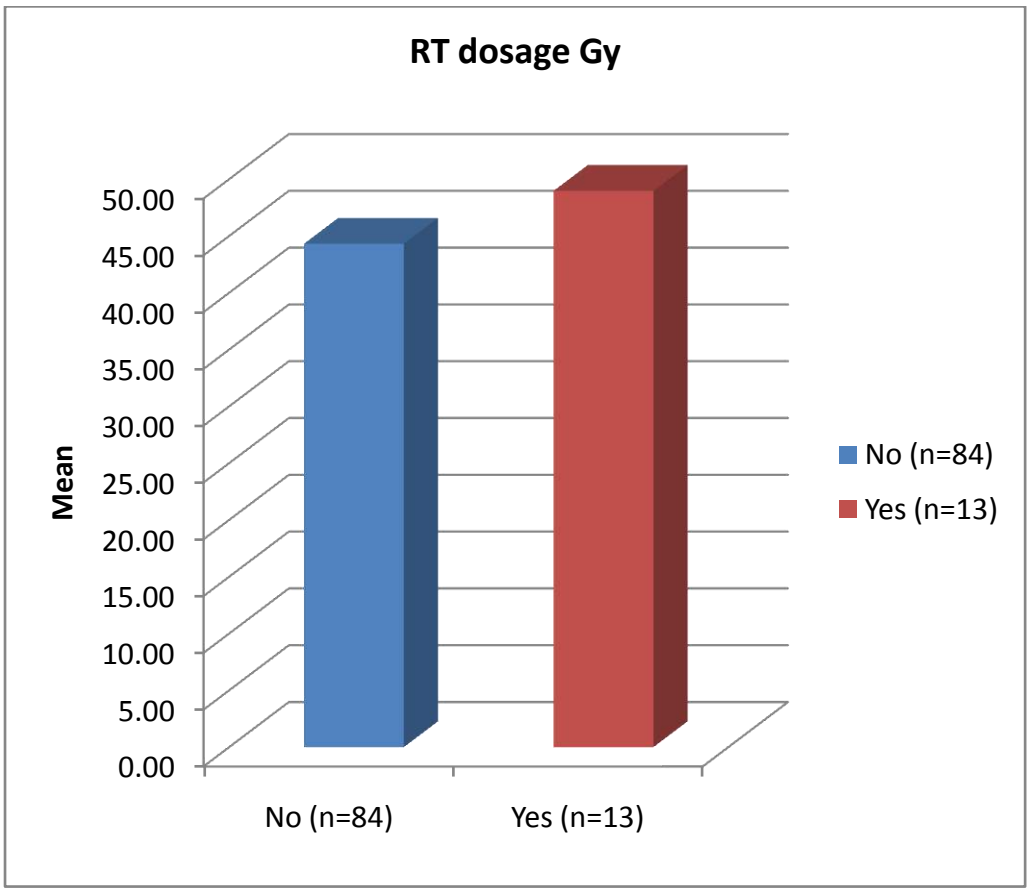



Figure 31: Mean radiotherapy wise among patients who developed LV dysfunction

Table 37: Mean radiotherapy wise among patients who developed LV dysfunction

| | No LVD (n=84) | | LVD (n=13) | | t/Z | p-value |
|---|---|---|---|---|---|---|
| | Mean | SD | Mean | SD | | |
| Doxorubicin | 367.08 | 85.84 | 301.67 | 153.17 | 1.860 | 0.068 |
| Cylophosphamide | 3676.48 | 898.58 | 3034.00 | 1467.40 | 1.864 | 0.067 |
| Trastuzumab | 2771.71 | 1128.55 | 1487.20 | 437.83 | 2.489 | 0.018 |
| Carboplatin | 2418.52 | 1175.35 | 1755.00 | 887.48 | 1.194 | 0.242 |
| Paclitaxel | 1215.85 | 586.78 | 1383.33 | 544.71 | -0.640 | 0.527 |
| Docetaxel | . | . | 507.50 | 112.36 | | |

In the present study there was no significant difference between two groups in term of distribution of Doxorubincin (P=0.068), Cyclophosphamide (P=0.067), Carboplatin (P=0.242) and Paclitaxel (P=0.527) .

In the present study there was significant difference between two groups in term of distribution of Trastuzumab (P=0.018).

Mean dose of Doxorubicin was 301.67 in LVD group while it was 367.08 in no LVD group.

Mean dose of Cyclophophamide was 3034 in LVD group while 3676.48 in No LVD group.

Mean dose of Trastuzumab was 1487.20 in LVD group and 2771.71 in No LVD group.

Mean of Paclitaxel was 1215.85 in LVD group and 1383.33 in LVD group.

Docetaxel was given only to LVD group and mean dose was 507.50

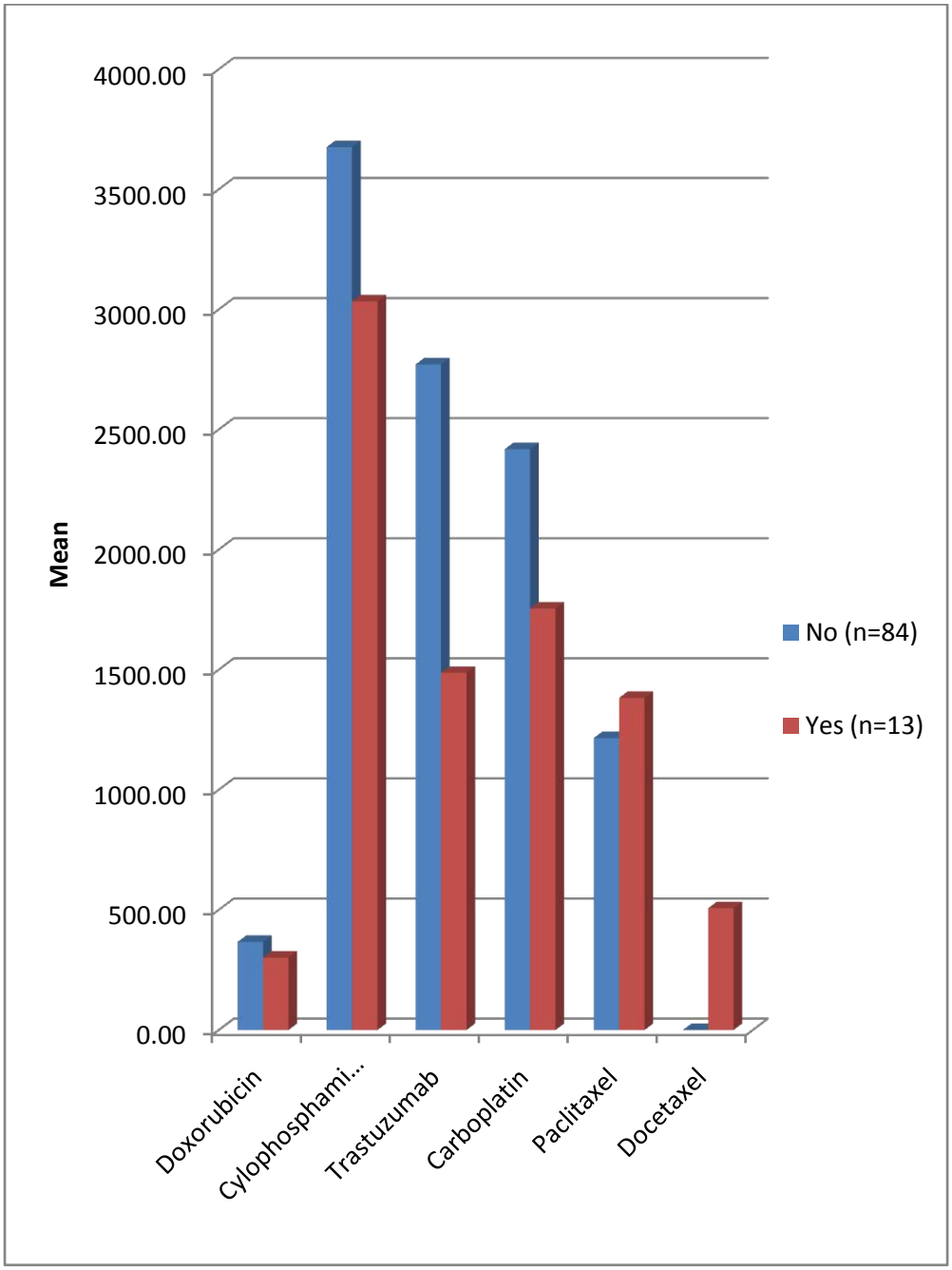



Figure 32: mean radiotherapy wise among patients who developed LV dysfunction

Table 38: Number of patients recovered from LV dysfunction

| LV Function EF % | No. of cases | Percentage |
|---|---|---|
| Not recovered | 3 | 23.1% |
| Recovered | 10 | 76.9% |
| Total | 13 | 100.0% |

Total 13 patients developed LV dysfunction out of10 (76.9%) patients recovered while 3(23.1%) remained in LV dysfunction.

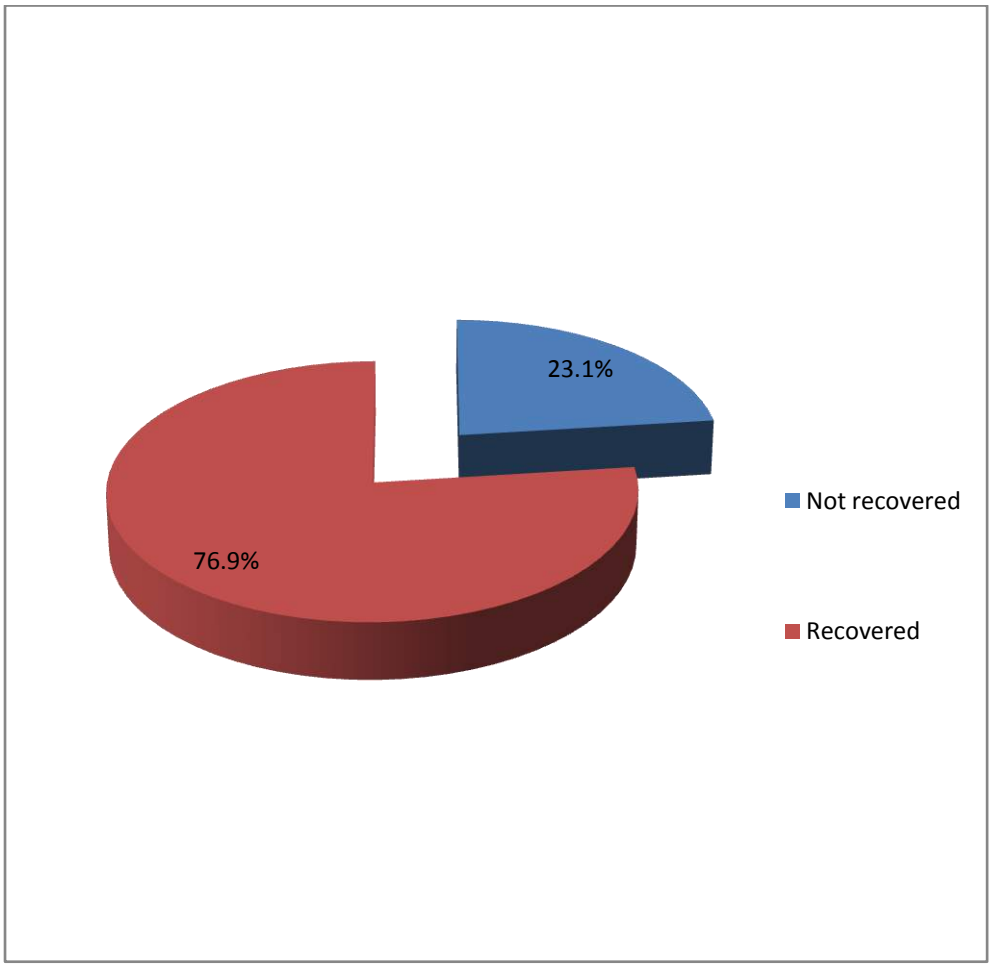



Figure 33: Number of patients recovered from LV dysfunction

Table 39: Serial Echocardiography of patients who developed LV Dysfunction.

| LVD (n=13) | First Echocardiography | | Second Echocardiography | | Third Echocardiography | | Fourth Echocardiography | |
|---|---|---|---|---|---|---|---|---|
| | Mean | SD | Mean | SD | Mean | SD | Mean | SD |
| LAVI | 34.38 | 0.77 | 33.46 | 0.78 | 34.69 | 1.75 | 33.69 | 1.97 |
| Aortic Root | 26.77 | 1.42 | 25.00 | 1.63 | 26.38 | 0.77 | 25.92 | 0.86 |
| LVID (S) | 33.85 | 0.55 | 34.08 | 0.95 | 34.15 | 0.90 | 34.46 | 0.97 |
| LVID (D) | 47.08 | 1.12 | 48.85 | 1.77 | 48.69 | 1.65 | 49.00 | 1.08 |
| IVST (S) | 9.15 | 0.38 | 9.08 | 0.28 | 9.08 | 0.28 | 9.08 | 0.28 |
| IVST(D) | 6.85 | 1.07 | 6.54 | 0.88 | 6.23 | 0.83 | 6.85 | 1.14 |
| LVPW(S) | 9.08 | 0.28 | 9.08 | 0.28 | 9.08 | 0.28 | 9.08 | 0.28 |
| LVPW(D) | 6.62 | 0.87 | 6.54 | 0.88 | 6.54 | 0.88 | 6.69 | 0.85 |
| EF(%) | 61.92 | 0.64 | 49.08 | 12.97 | 43.46 | 4.05 | 53.15 | 6.39 |
| GLS(%) | -19.18 | 1.20 | -15.83 | 3.51 | -14.46 | 1.52 | -17.57 | 2.45 |
| GCS (%) | -24.12 | 1.65 | -20.58 | 2.80 | -19.92 | 1.45 | -22.12 | 2.09 |
| MAPSE | 12.92 | 1.12 | 10.38 | 2.02 | 9.31 | 0.75 | 10.85 | 1.41 |
| DT(ms) | 192.46 | 5.61 | 225.38 | 18.98 | 229.69 | 11.74 | 209.38 | 11.06 |
| e'(cm/s) | 10.23 | 0.60 | 8.62 | 1.94 | 8.77 | 1.01 | 9.77 | 1.30 |
| s'(cm/s) | 11.85 | 0.55 | 10.15 | 2.27 | 8.88 | 0.70 | 11.77 | 0.93 |
| E/e' | 4.23 | 0.60 | 11.92 | 2.10 | 10.08 | 2.25 | 7.85 | 2.08 |
| PASP | 0.00 | 0.00 | 3.69 | 9.16 | 6.23 | 10.79 | 2.54 | 6.23 |

Mean Ejection fraction before starting chemotherapy was 61.9%. Echocardiography done at mid of chemotherapy shows mean Ejection fraction of 49 %. While, Echocardiography done at end of chemotherapy, revealed mean ejection fraction of 43.4%. The patient who developed LV dysfunction was further followed up with fourth echocardiography after 3 months shows mean ejection fraction of 53.15%.

On the hand, GLS and GCS during first echo was -19.18 and -24.12, during second echo it was -15.83 and -20.58, while during third echo it was -14.46 and -19.92, and during fourth echo it was -17.57 and -22.12 respectively.

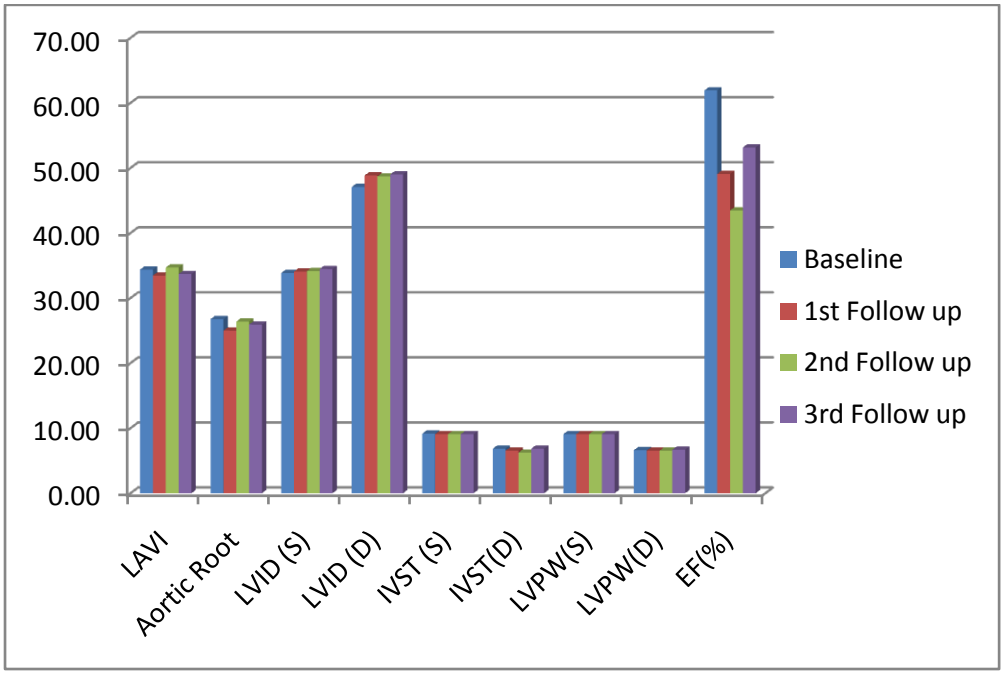



Figure 34 A: Serial Echocardiography of patients who developed LV Dysfunction.

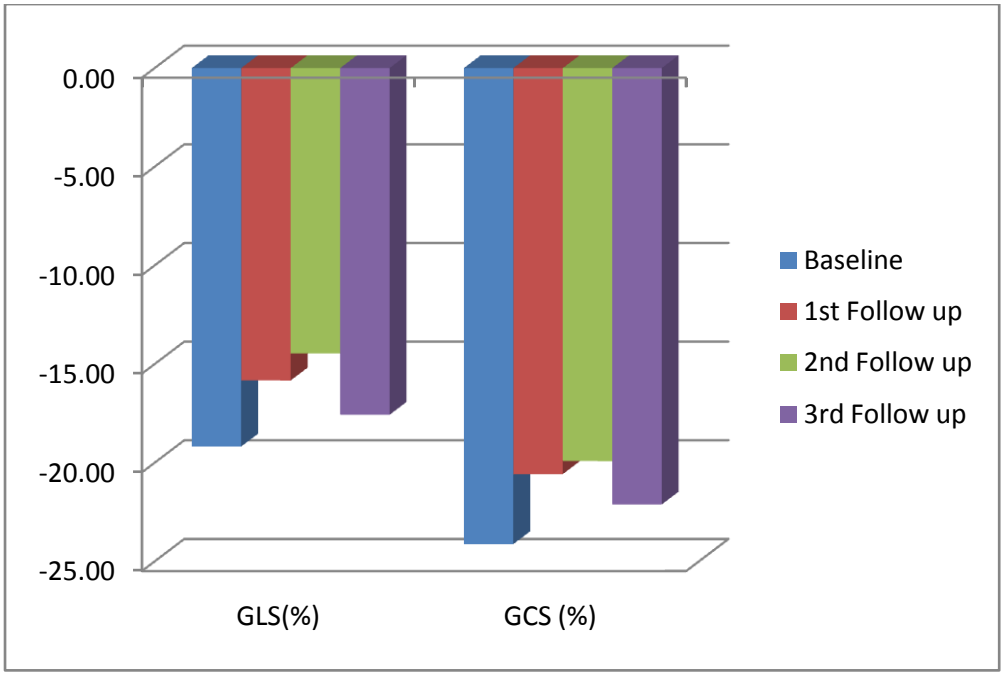



Figure 34 B: Serial Echocardiography of patients who developed LV Dysfunction.

Table 40: Serial Echocardiography of patients who developed LV Dysfunction.

| | First Echocardiography | Second Echocardiography | Third Echocardiography | Fourth Echocardiography |
|---|---|---|---|---|
| Total LVD | 0 | 6 | 13 | 3 |
| New LVD | 0 | 6 | 7 | 0 |
| DD 1 | 0 | 2 | 3 | 2 |
| Mild LVD | 0 | 1 | 11 | 2 |
| Moderate LVD | 0 | 4 | 2 | 1 |
| Severe LVD | 0 | 1 | 0 | 0 |
| Completely recovered | 0 | 0 | 0 | 10 |
| Partially recovered | 0 | 0 | 6 | 3 |

Total LVD in second echocardiography were 6 and in third echocardiography were 13. Out of which 3 recovered and 10 remained in LVD. Out of 13, 11 were having mild LVD, 2 were in moderate LVD and no patient in severe LVD during third echocardiography. Diastolic dysfunction grade 1 was present in 3 patients during third echocardiography.

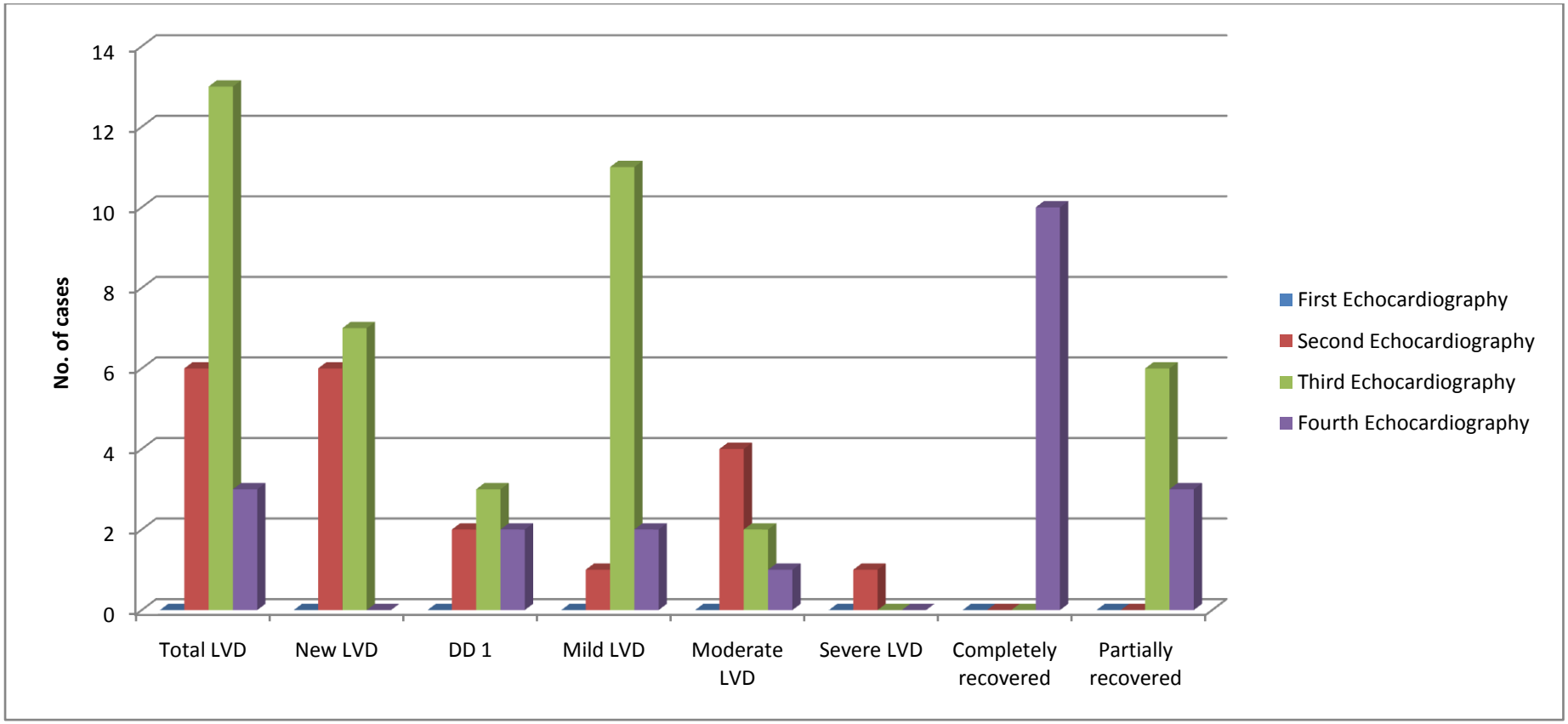



Figure 35: Serial Echocardiography of patients who developed LV Dysfunction.

Table 41: Drugs used in LVD group

| Drugs | No. of cases | Percentage |
|---|---|---|
| RAS INHIBITORS | 13 | 100.0% |
| B Blockers | 13 | 100% |
| Diuretic | 1 | 7.7% |
| MRA | 1 | 7.7% |

Out of 13 patients who developed LVD, all patients received 13 (100%) received RAS inhibitors.

13 (100%) patients received b blockers, Diuretic and MRA prescribed in only 1 patient (7.7%).

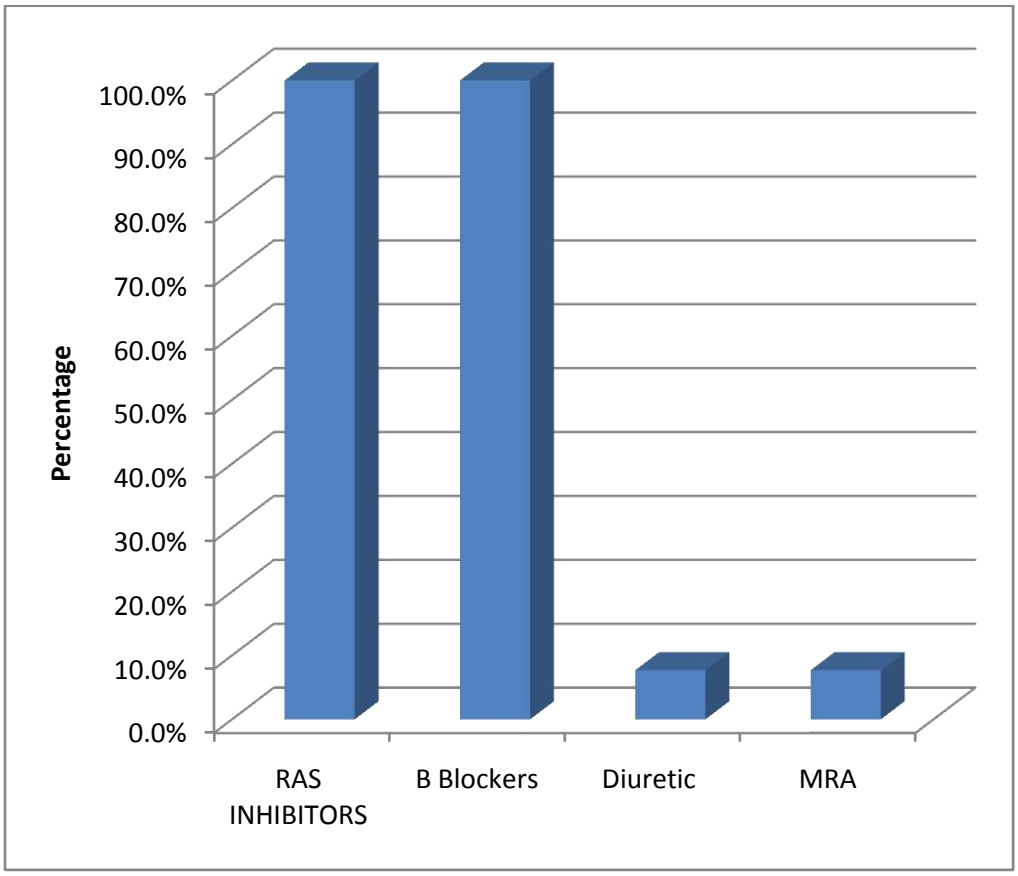



Figure 36: Drugs used in LVD group

Table 42: Characteristics of patients who recovered from LV dysfunction

| | | Full Recovery | | Partial recovery | | Total |
|---|---|---|---|---|---|---|
| | | No. of cases | %age | No. of cases | %age | |
| Age group | 1 | 4 | 40.0% | 2 | 66.7% | 6 |
| | 2 | 5 | 50.0% | 0 | 0.0% | 5 |
| | 3 | 1 | 10.0% | 1 | 33.3% | 2 |
| HTN | No | 9 | 90.0% | 2 | 66.7% | 11 |
| | yes | 1 | 10.0% | 1 | 33.3% | 2 |
| surgical extent | Left | 8 | 80.0% | 3 | 100.0% | 9 |
| | Right | 2 | 20.0% | 0 | 0.0% | 2 |

Out of 13 patients, 10 (76.9%) patients recovered completely while 3 (23.07%) remained in LV dysfunction group.

5 (50%) patients in complete recovery group was b/w 51 to 60 years of age group, 4 (40%) patients from < 50 years and 1 (10%) patient from > 60 years of age group.

In partial recovery group, 2 (66.6%) patients belong to age group < 50 years while 1 (33.33%) patient patients belong to > 60 years of age group.

In both the group, one patient was hypertensive. In full recovery group 1 (10%) patients were hypertensive while in partial recovery group 1 (33.33%) were hypertensive.

Left sided breast involvement seen in 8 (80%) and 3 (100%) patients in full recovery and partial recovery group respectively.

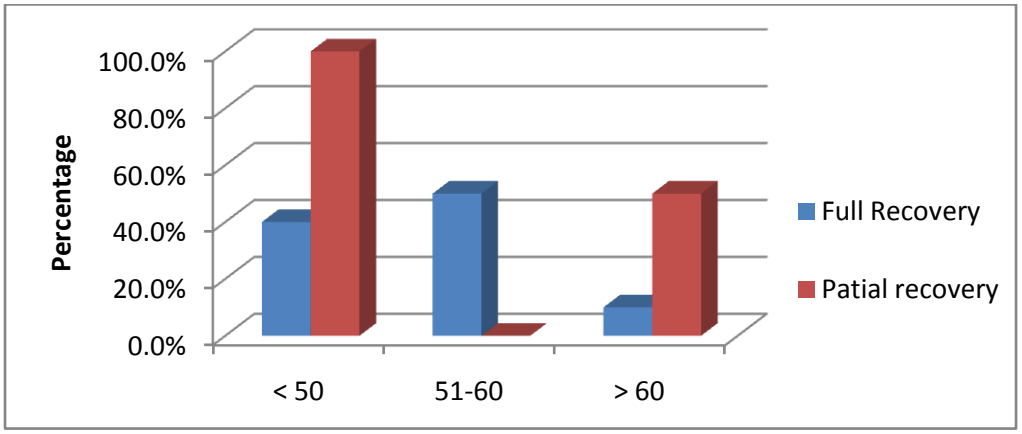



Figure 37 A: Characteristics of patients who recovered from LV dysfunction.

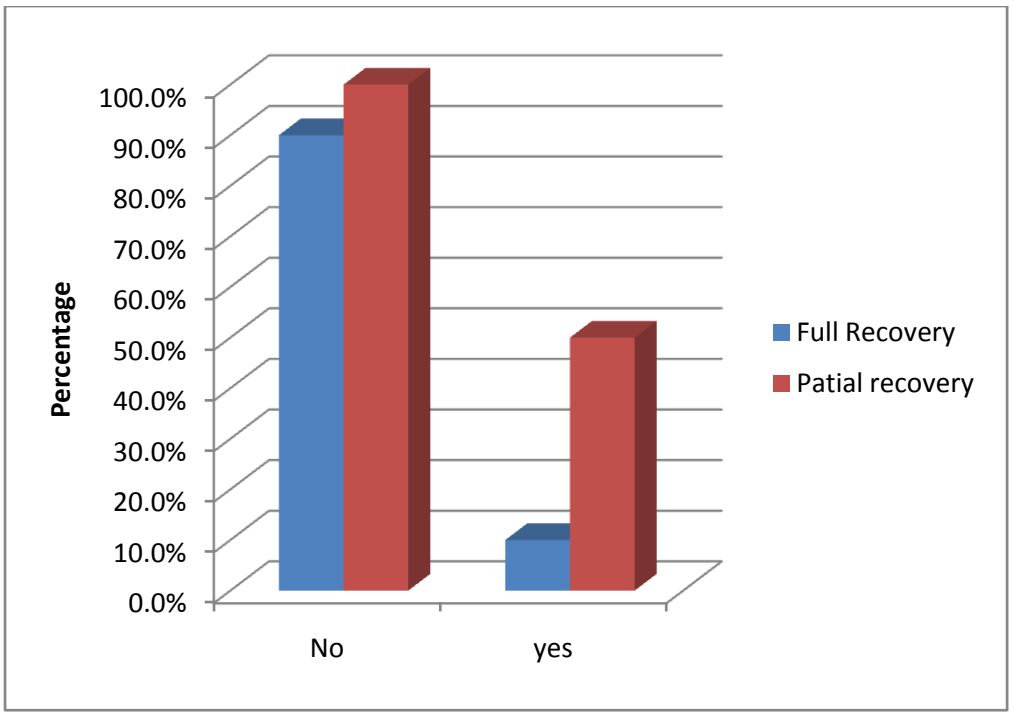



Figure 37 B: Characteristics of patients who recovered from LV dysfunction.

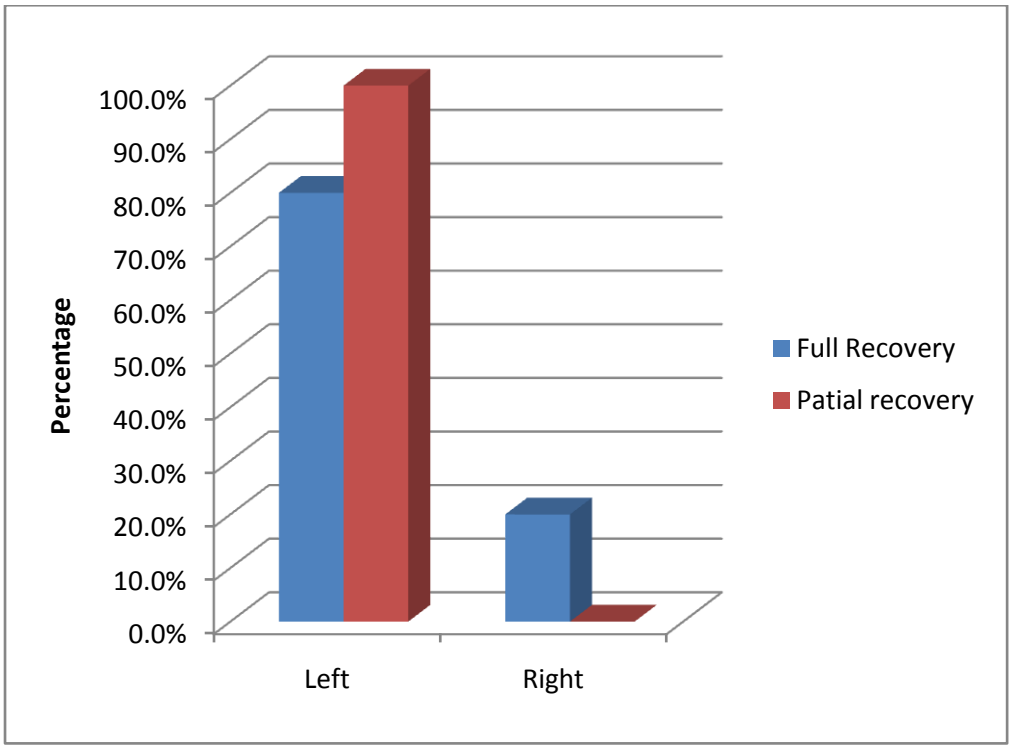



Figure 37 C: Characteristics of patients who recovered from LV dysfunction.

Table 43: Characteristics of patients who were completely and partially recovered from LV dysfunction

| | | Complete Recovery (10) | | Partial recovery (3) | | Total |
|---|---|---|---|---|---|---|
| ER+ | Negative | 8 | 80.0% | 2 | 66.66% | 10 |
| | Positive | 2 | 20.0% | 1 | 33.33% | 3 |
| PR+ | Negative | 7 | 70.0% | 3 | 100.0% | 10 |
| | Positive | 3 | 30.0% | 0 | 0.0% | 3 |
| HER2+ | Negative | 5 | 50.0% | 2 | 66.66% | 7 |
| | Positive | 5 | 50.0% | 1 | 33.33% | 6 |
| Cancer Stage | II | 4 | 40.0% | 0 | 0.0% | 4 |
| | III | 5 | 50.0% | 2 | 66.66% | 7 |
| | IV | 1 | 10.0% | 1 | 33.33% | 2 |
| T | 1 | 2 | 20.0% | 0 | 0.0% | 2 |
| | 2 | 3 | 30.0% | 2 | 66.66% | 5 |
| | 3 | 2 | 20.0% | 1 | 33.33% | 3 |
| | 4 | 3 | 30.0% | 0 | 0.0% | 3 |
| N | 0 | 1 | 10.0% | 0 | 0.0% | 1 |
| | 1 | 5 | 50.0% | 1 | 33.33% | 6 |
| | 2 | 3 | 30.0% | 1 | 33.33% | 4 |
| | 3 | 1 | 10.0% | 1 | 33.33% | 2 |
| M | 0 | 10 | 100.0% | 2 | 66.66% | 12 |
| | 1 | 0 | 0.0% | 1 | 33.33% | 1 |
| Total | | 10 | 100.0% | 3 | 100.0% | 13 |

2 (20%) patients in full recovery and 1 (33.33%) patients in partial recovery patients were ER positive. 3 (30%)patients from full recovery group was PR positive, while in partial recovery no patient was PR positive. 5 (50%) patients in full recovery and 1 (33.33%) patient in partial recovery group were HER 2 positive.

5 (50%) patients and 4 (40%) patients in full recovery belongs to stage III and II respectively and only one patient belongs to stage IV.While in partial recovery group 2 (66.66%) patients were in stage III and one patient in stage IV.

3 (30%) patients belong to T4 and T2 in full recovery group and only 2 (20%) patients belong to T3. While in partial recovery, 2 (66.66%) patients were in T2 and one (33.33%) patient in T3 stage.

In full recovery group, 5 (50%) patients were in N1, 3 (30%) patients in N2 and one (10%) patient in N3. While in partial recovery each one patient (33.33%) belongs to N1, N2 and N3 stage.

Only one patient in partial recovery group belongs to M1 stage.

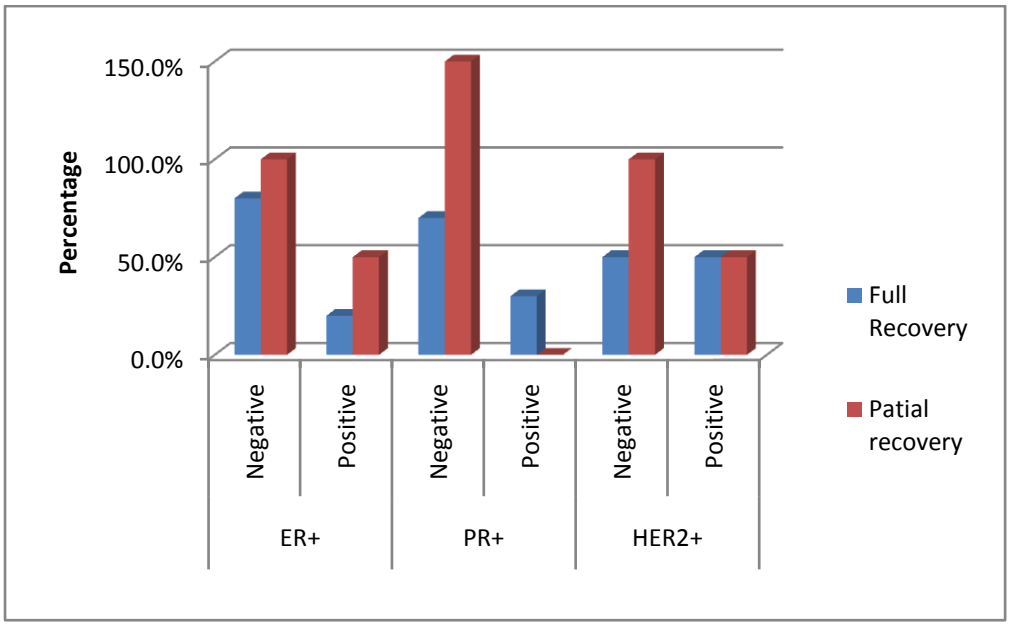



Figure 38 A: Characteristics of patients who were completely and partially recovered from LV dysfunction.

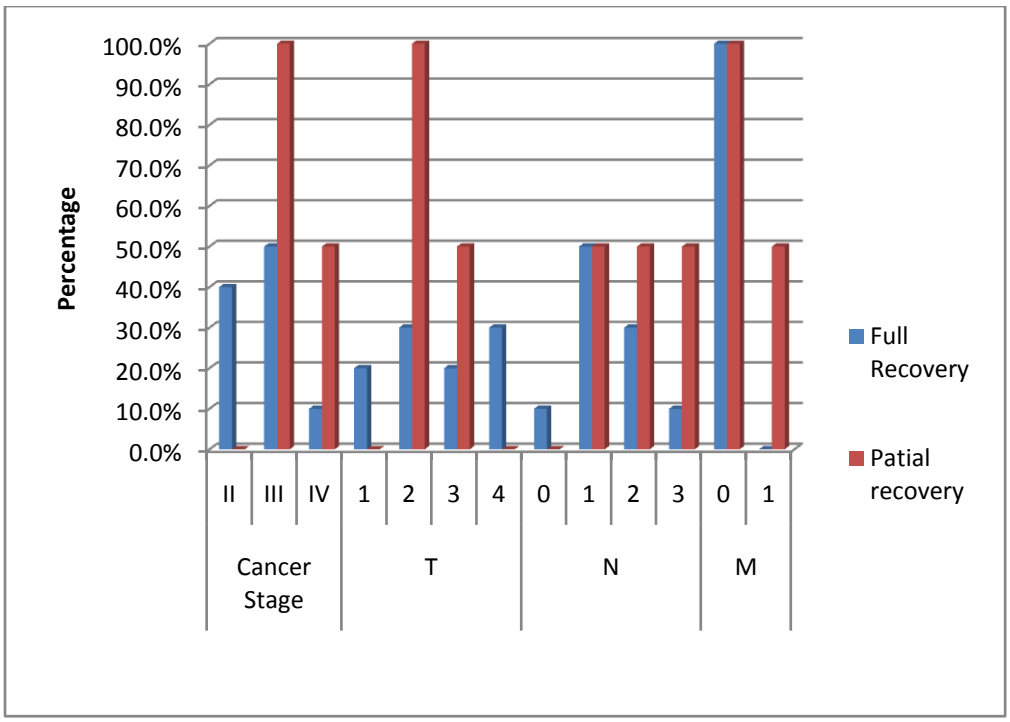



Figure 38 B: Characteristics of patients who were completely and partially recovered from LV dysfunction.

Table 44: Characteristics of patients who were completely and partially recovered from LV dysfunction

| | Complete Recovery (10) | | Partial recovery n=3 | |
|---|---|---|---|---|
| | Mean | SD | Mean | SD |
| Age | 58.00 | 14.14 | 49.60 | 7.28 |
| Haemoglobin | 10.82 | 1.23 | 11.10 | 0.69 |
| Albumin | 3.92 | 0.38 | 3.99 | 0.21 |
| BMI | 31.49 | 6.19 | 23.82 | 4.58 |
| BSA | 1.63 | 0.15 | 1.68 | 0.13 |
| RT dosage Gy | 50.16 | 0.22 | 46.00 | 8.49 |
| Doxorubicin | 306.43 | 135.98 | 285.00 | 275.77 |
| Cylophosphamide | 3067.50 | 1272.49 | 2900.00 | 2828.43 |
| Trastuzumab | 1487.20 | 437.83 | . | . |
| Carboplatin | 2075.00 | 1088.86 | 1275.00 | 106.07 |
| Paclitaxel | 1070.00 | 294.62 | 2010.00 | 212.13 |
| Docetaxel | 507.50 | 112.36 | . | . |

Mean age in full recovery group was 58 and 49.60 in partial recovery group.

Mean haemoglobin was 10.8 and 11.10 in complete recovery and partial recovery group respectively.

Mean albumin in full recovery was 3.92 in complete recovery group and 3.99 in partial recovery group.

Mean BMI was 31.49 in complete recovery and 23.83 in partial recovery group.

Mean BSA in complete recovery group was 1.63 while it was 1.68 in partial recovery group.

Mean Radiotherapy dose in complete recovery group was 50.16 and 46 in partial recovery group.

Mean dose of doxorubicin was 306.43 in complete recovery group while it was 285 in partial recovery group.

Mean dose of Cyclophosphamide was 3067.50 in complete recovery group and 2900 in partial recovery group.

Mean dose of paclitaxel was 2010 in partial recovery and 1070 in complete recovery group.

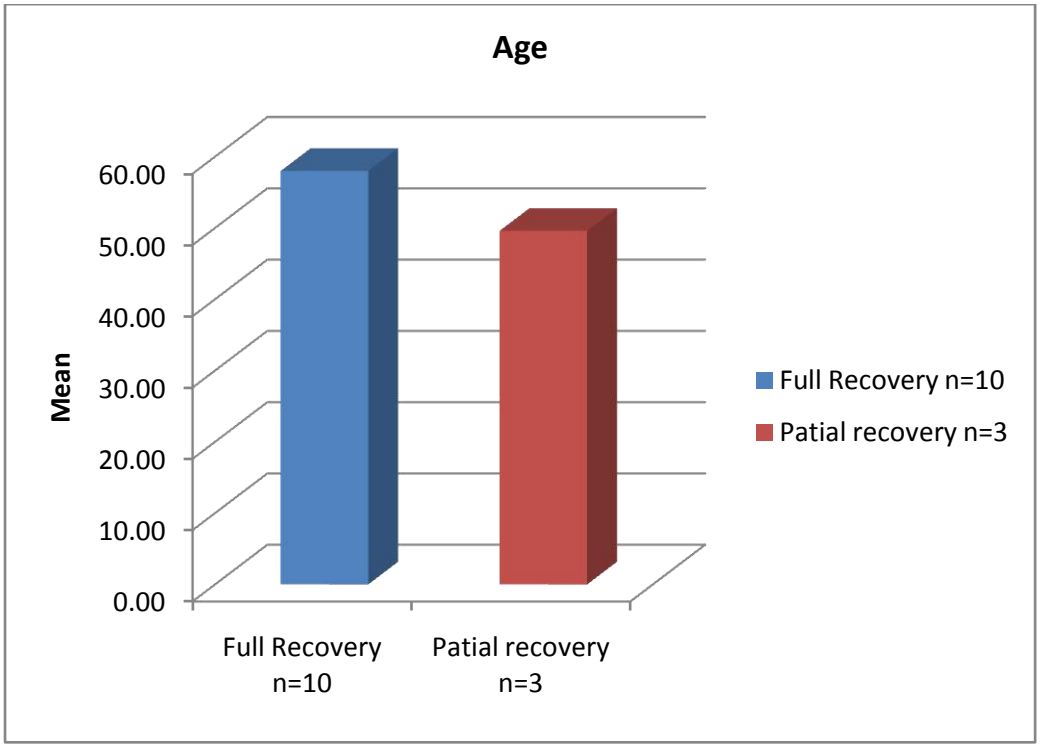



Figure 39 A: Characteristics of patients who were completely and partially recovered from LV dysfunction

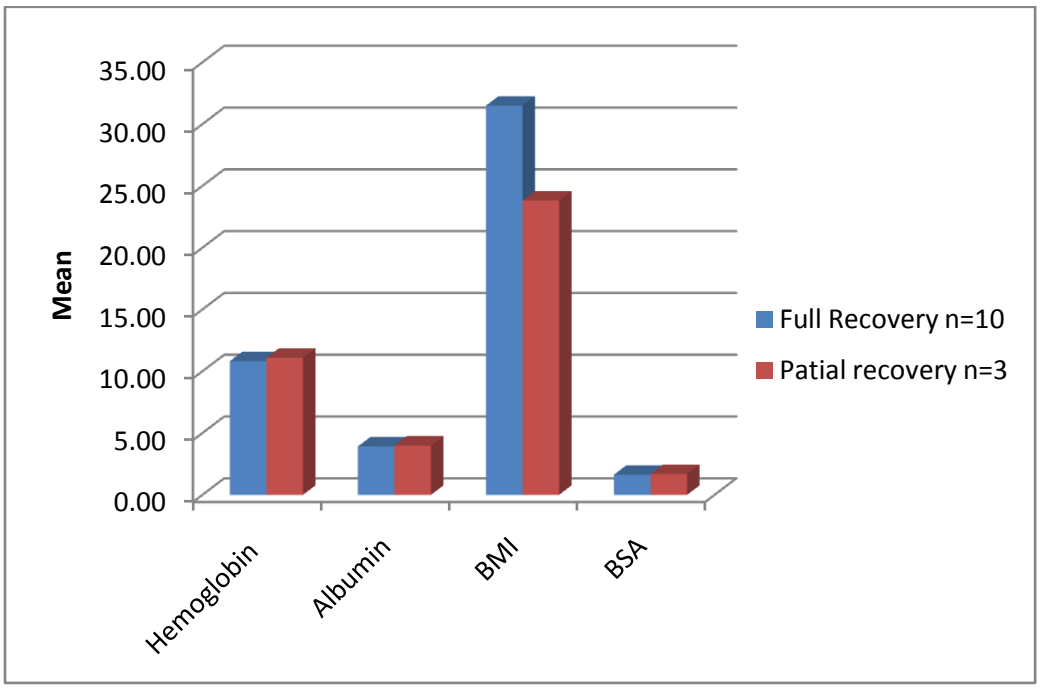



Figure 39 B: Characteristics of patients who were completely and partially recovered from LV dysfunction

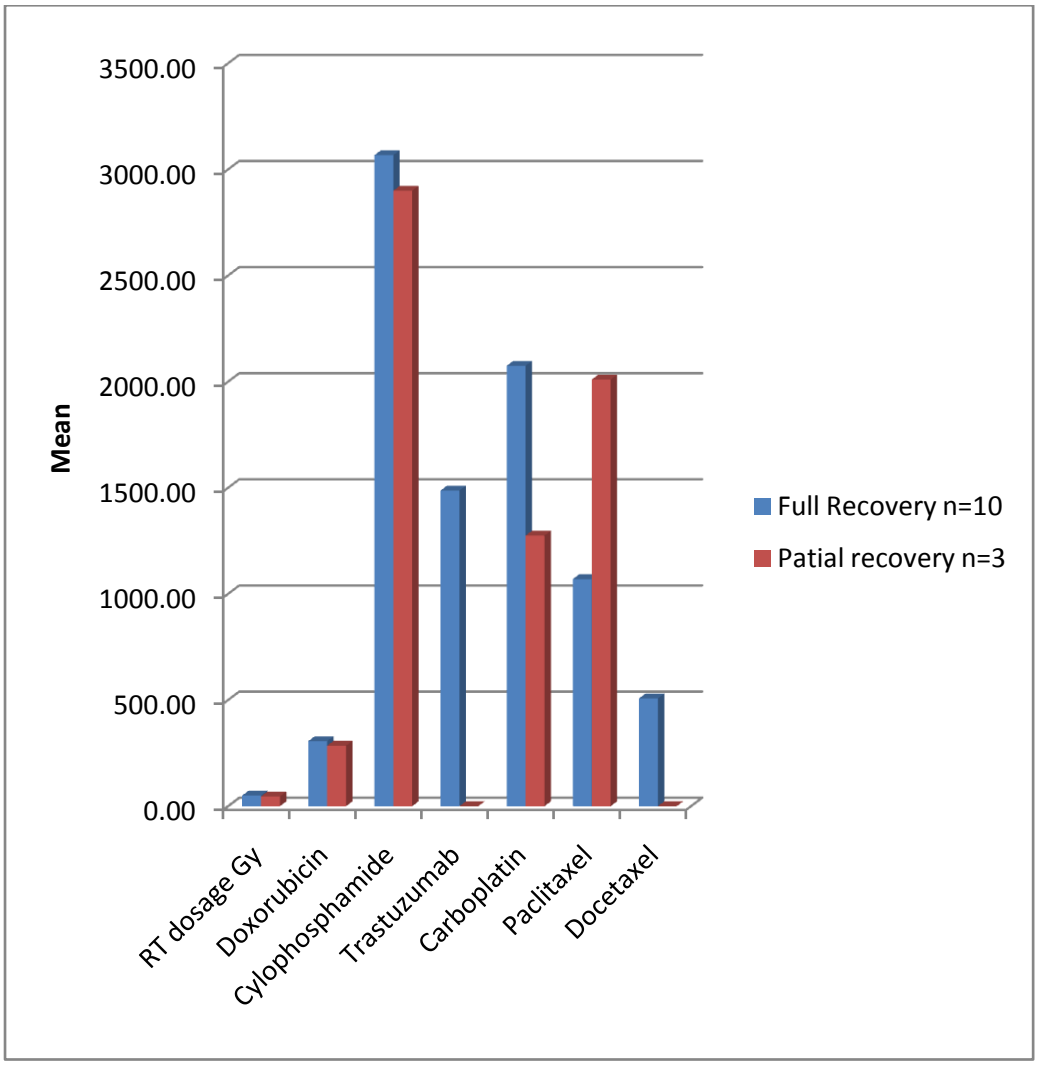
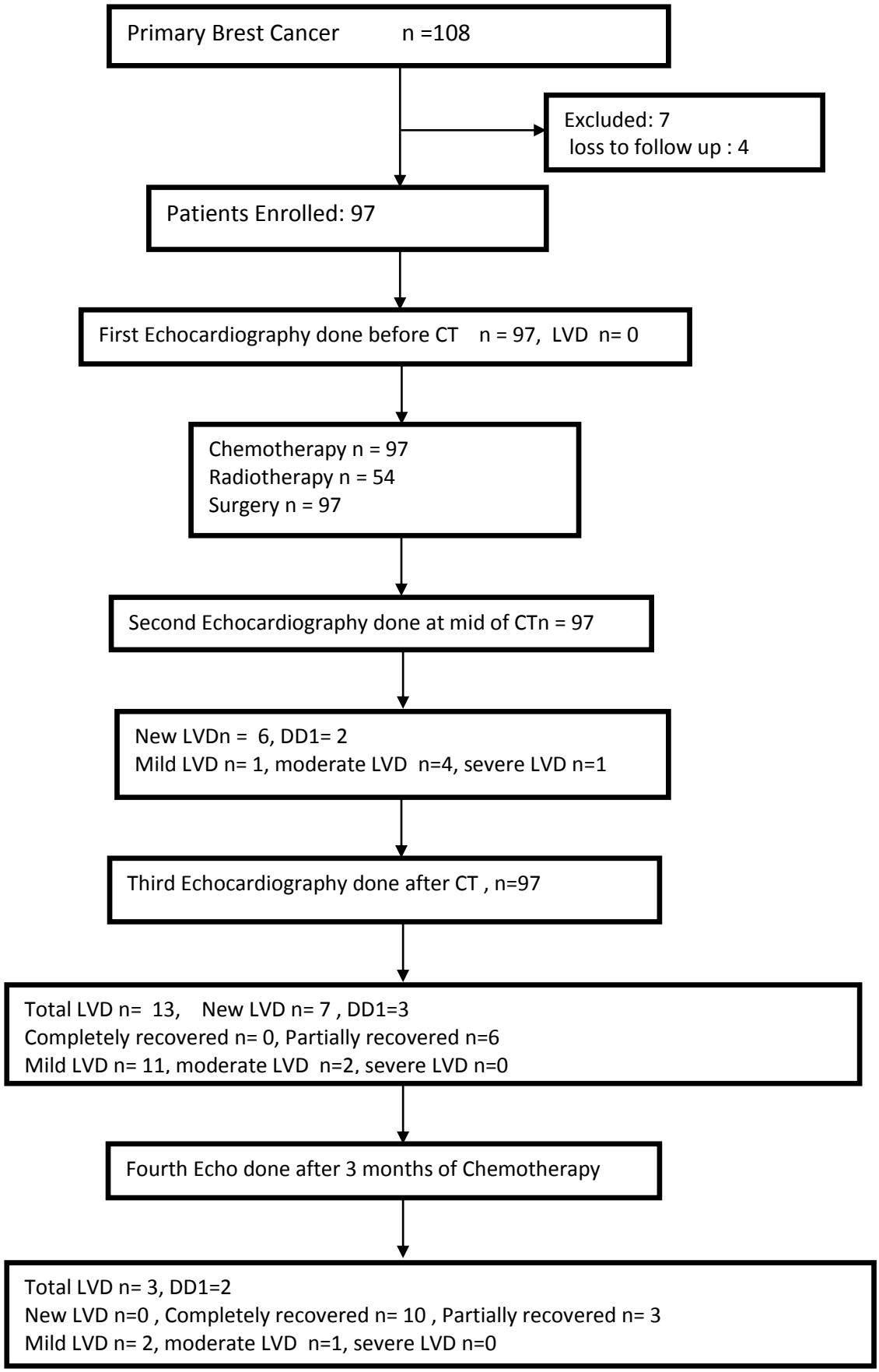



Figure 39 C: Characteristics of patients who were completely and partially recovered from LV dysfunction

## FLOW CHART


Primary Brest Cancer n =108
Excluded: 7
loss to follow up : 4
Patients Enrolled: 97
First Echocardiography done before CT n = 97, LVD n= 0
Chemotherapy n = 97
Radiotherapy n = 54
Surgery n = 97
Second Echocardiography done at mid of CTn = 97
New LVDn = 6, DD1= 2
Mild LVD n= 1, moderate LVD n=4, severe LVD n=1
Third Echocardiography done after CT , n=97
Total LVD n= 13, New LVD n= 7 , DD1=3
Completely recovered n= 0, Partially recovered n=6
Mild LVD n= 11, moderate LVD n=2, severe LVD n=0
Fourth Echo done after 3 months of Chemotherapy
Total LVD n= 3, DD1=2
New LVD n=0 , Completely recovered n= 10 , Partially recovered n= 3
Mild LVD n= 2, moderate LVD n=1, severe LVD n=0

# DISCUSSION

In the present study we evaluated chemotherapeutics related cardiac dysfunction in patient with breast cancer. There are very few studies available in the literature predicting the incidence of acute cardiac toxicity of chemotherapy in breast cancer patients. Most of the studies have long term follow up of more than one years which includes early and late toxicity of chemotherapy. To our knowledge this the first study in India on acute cardiac toxicity of chemotherapy.

Cardio-oncology is a new field of interest in cardiology that focuses on the detection, monitoring, and treatment of cardiovascular disease occurring as a side effect of chemotherapy and radiotherapy. Advances in treatment of cancer have led to improved survival but have also increased morbidity and mortality due to treatment related side effects. Cardiovascular diseases are the most frequent and serious of these side effects which are a matter of growing concern among Cardio oncologist. Therefore it is necessary to periodically monitor cancer patients under treatment, especially those receiving anthracyclines and trastuzumab using mainly echocardiography or MUGA Scan. Thus Chemotherapy is now proved to be 'Double Edged Sword'. Cancer patients who were successfully treated with chemotherapy are suffering from cardiovascular diseases. For instance, anthracyclines, trastuzumab and some tyrosine kinase inhibitors have detrimental effect on myocardial function.

Total 108 newly diagnosed breast cancer patients who came to oncology wing of tertiary care hospital were initially enrolled. After exclusion of 7 patients, 97 patients were finally enrolled. The reason for the exclusion of patients were advanced metastatic disease with multi-organ failure, LV ejection fraction less than 55% on baseline echocardiography, and who had received chemotherapy before. 4 patients were loss to follow up after initial radiotherapy. We evaluated LV function using echocardiography and global longitudinal strain

before starting chemotherapy and then, serial follow up at mid of chemotherapy and at the end of chemotherapy was done.

In the present study all the patient underwent surgery. After surgery patients were assessed by oncologist and radiotherapy specialist for the need of radiotherapy. All the eligible patients received radiotherapy before starting the chemotherapy. 55.7% patients underwent radiotherapy. Following 2-3 weeks of radiotherapy, all patient underwent baseline echocardiography, before starting chemotherapy. Chemotherapy was administered in 4-6 cycles as determined by treating oncologist. Second echocardiography was performed at the mid of chemotherapy and third echocardiography at the end of chemotherapy. In Hyun J Y et al study[22] (2016) in which they studied the chemotherapy induced LV dysfunction in patients with breast cancer on 712 patients, 93% patients received Radiotherapy. Baseline echocardiography was performed before starting chemotherapy and follow up echocardiography was performed just after finishing all schedules of chemotherapy regimen. In Anita Boyd et al study[20] (2017) in which they studied anthracyclines induced early changes in LV systolic and diastolic function on 140 patients, echocardiography was done before and within 7 days of post treatment.

For screening, risk stratification and early detection first step is to identify patients at increased risk of cardio toxicity consist of careful baseline assessment of cardiovascular risk factors. A very limited number of studies have generated risk scores for different oncology patients. Risk assessment includes careful clinical history, physical examination and baseline measurement of cardiac function either by echocardiography or MUGA scan. According to ASCO- 2019 and 2018 (American Society of Clinical Oncology), ESMO-2017 and 2020 (the European Society of Medical Oncology), and the ESC-2016 (European Society of Cardiology) before chemotherapy history, examination, ECG and echocardiography with GLS should be done. And during chemotherapy, patients receiving high dose of anthracycline with

baseline risk factors should be screened with echo with GLS, cardiac biomarkers and ECG.

In the present study we did risk assessment by taking detailed history of cardiovascular risk factors including Diabetes mellitus, hypertension, family history; clinical examination, vitals assessment, BMI, BSA, haemoglobin, albumin, renal function test, cancer staging, TNM classification and baseline echocardiography. ECG, lipid profile and Cardiac biomarkers like BNP and troponin was not performed for all patients. In Hyun J Y et al and Anita Boyd et al study cardiac biomarkers and ECG was not performed. In literature use of cardiac biomarkers may be considered in order to detect early cardiac injury. There is no clear-cut evidence to withhold or interrupt chemotherapy based on abnormal cardiac biomarkers. However, an abnormal biomarkers result is indicative of increased risk of cardio toxicity. Patients treated with trastuzumab, particularly who are exposed to previous anthracyclines , troponin I elevation clearly identify patients who will develop cardiac dysfunction and will not recover despite HF treatment. In D cardinal et al study[10] (2000), on 204 patient's troponin I was done after every cycle of chemotherapy patients in whom troponin I was positive had marked reduction of LVEF and persist at end of follow up.

Chemotherapy drugs used in the present study were Doxorubicin, Cyclophosphamide, Trastuzumab, carboplatin and paclitaxel. One chemotherapy drug was received by 6.1% patients; two drugs were received by 59.7% patients, three drugs by 21.6% patients and four drugs combination by 12.4% patients. 63.9% patients received Doxorubicin, 65.6% patients received Cyclophosphamide, 37% patients received Trastuzumab, 32.9% patients received Carboplatin and 34% patients received paclitaxel. In Hyun J Y et al study they studied Doxorubicin (23%), Epirubicin (25%), cyclophosphamide (58%) and paclitaxel (24.7%), while in Anita Boyd et al study that included only anthracyclines i.e. doxorubicin or epirubicin and no patient received trastuzumab and radiotherapy.

Incidence of acute cardio toxicity was 13.4% in the present study. In Hyun J Y et al incidence of LVD was 11.5% and in Anita Boyd et al study, LVEF remained within normal range i.e. 60% in baseline and 59% after treatment, while subclinical LVD which was defined as relative decrease of GLS > 11% from baseline occurred in 22% patients. In the present study Cardio toxicity was be defined as a decrease in LVEF > 10 percentage points from the baseline or < 50%; subclinical LVD is relative decrease from baseline in global longitudinal strain (GLS) > 15 %. [26] In Hyun J Y et al study LV dysfunction defined as LVEF < 55% or decrease in LVEF of > 10% from baseline.In the present study 46.2% patients detected as LV systolic dysfunction on second echocardiography i.e. during mid of the chemotherapy and 53.8% patients developed LV systolic dysfunction on third echocardiography i.e. at the end of chemotherapy. 84.6% patients had mild LV systolic dysfunction (EF= 41-50%), 15.3% patients had moderate LV systolic dysfunction (EF=31-40%) and 7.6% patient had severe LV systolic dysfunction (EF< 30%).

Diastolic dysfunction grade 1 was developed in 23% patients. In Hyun J Y et al study advanced diastolic dysfunction of >2 grade was significantly increased not only in LVD group (2.4% vs 11.2%) but also in no LVD group (1.4% vs 12.7%).In Anita Boyd et al impaired diastolic dysfunction grade significantly increased from 46% to 57% after treatment. Diastolic dysfunction was more common in subgroups with reduced systolic GLS compared to those without change in GLS (30% vs 11%). In literature, diastolic dysfunction is common in cancer patients both at base line and during treatment, however there no evidence to stop treatment based on these findings. In Jenica et al study[30] (2020), in which they study 362 patients of breast cancer who received doxorubicin and trastuzumab; abnormal diastolic function grade occurred in 60% at 1 year, 70% by 2 years, and 80% by 3 years. Abnormal diastolic function grade was associated with a subsequent decrease in LVEF (-2.1%; 95% confidence intervals [CI]: -3.1 to -1.2; p

< 0.001) and worsening in longitudinal strain (0.6%; 95% CI: 0.1 to 1.1; p = 0.013) over time.

There was low level of evidence supporting cardiovascular side effects of chemotherapy that has led to numerous discrepancies between cardiologist and oncologists. On account of this recently different guidelines published which include ASCO- 2019 and 2018 (American Society of Clinical Oncology), ESMO-2017 and 2020 (the European Society of Medical Oncology), and the ESC-2016 (European Society of Cardiology). All the guidelines have given detailed information regarding cardio vascular toxicities which provide more practical approach towards diagnosis and management for physicians who take care of cancer patients. According to these guidelines patients who are at high risk of developing cardiac toxicity are patients who receive high dose of anthracyclines ( Doxorubicin ≥250 mg/$m^2$), female gender, age > 65 years or < 18 years, high dose of radiotherapy (≥ 30 Gy) , concomitant treatment with trastuzumab, pre-existing cardiac diseases, ≥ 2 risk factors including smoking, hypertension, diabetes mellitus, dyslipidaemia , CKD and obesity.

In our study mean age was 50.74 years, mean Haemoglobin 10.58 g/dL, mean BMI 27.89 Kg/$m^2$, mean radiotherapy 44.92 Gy, mean dose of Doxorubicin was 357, Trastuzumab 2593,paclitaxel 1246mg.

In the present study mean age in LVD group was 50.44 and 50.77 in no LVD group. In Hyun J Y et al study mean age in LVD group was 56.7 and in no LVD group 55.6. In the present study 15.4% in LVD group and no patient was hypertensive in No VD group. In Hyun J Y et al study 17.1% in LVD group and 23.5% in no LVD group were hypertensive. BMI in the present study was 29.72 in LVD group while 27.60 Kg/$m^2$ in no LVD group. In Hyun J Y et al BMI was 22.1 in LVD group and 23.6 in no LVD group. There was no diabetic, smoker and CKD patient in the present study. In Hyun J Y et al 8.5% in LVD and 9.7 % in No LVD group were Diabetic. In Anita Boyd et al study mean age was 52, 22 % patients were hypertensive, 6% were diabetic, 25%

smoker, 19% with dyslipidaemia and 32% having family history of CV disease.

Radiotherapy is also associated with cardio toxicity. Some studies found relative risk of fatal cardiovascular events between 1 and 2.2 in patients with breast cancer. In patient with breast cancer treated in the era of 1980-2000, the risk of cardio toxicity was highest in patients with both left breast radiotherapy and chemotherapy suggesting synergistic effects on cardiac risk. Marked interstitial myocardial fibrosis is common in radiotherapy induced cardio toxicity. Systolic dysfunction is generally observed when radiotherapy is combined with anthracyclines. Catherine jaworski et al[27](2013) found relative risk of cardiac toxicity of radiotherapy is between 1-2.2 % in patients with breast cancer. In valentine walker et al[28] (2019) study in which they performed echocardiography at base line and after 6 months of radiotherapy. They found that there was no significant decrease in LVEF , but mean decrease of 6 % GLS at 6 months , more with left sided breast involvement i.e. 48% compared to right breast which was 40%.

Radiotherapy was received by total 55.7% patients in the present study. 53.8% in LVD group and 56% patients in no LVD group received Radiotherapy. Mean dose of radiotherapy in LVD group was 48.97 and 44.32 Gy in no LVD group. In Hyun J Y et al study 85.3% patients in LVD group and 94.2% patients in no LVD group received radiotherapy. Mean dose of radiotherapy in LVD group was 53.6 and 56.8Gy in no LVD group. In our study mean dose of radiotherapy was higher in LVD group but in Hyun et al study mean dose of radiotherapy was lower in LVD group.

Patients in Cancer stage III, among LVD group were present in 54% compared to 42% in No LVD group. 15.4% patient in LVD group and 5 % patients in no LVD group were in stage IV. In Hyun J Y et al[22] (2016) study 48.8% patients were in cancer stage III-IV and 22% in No LVD group. In the literature advanced cancer stage is not the predictor

of LV dysfunction but result of our study was similar to Hyun J Y et al study.

23% patients in LVD group were ER positive compared to 3.6% in no LVD group in the present study. 23 % patients in LVD were PR positive compared to 13 % in no LVD group.46% patient were HER2 positive compared to 37% in no LVD group. In Hyun J Y et al[22] ( 2016) study ER positive seen in 48.8% patients in LVD group and 70 % patients in no LVD group, PR positive in 44% in LVD group vs 66.8% in no LVD group and HER2 positive in 82.9% vs 72% in no LVD group. In Hyun J y et al study percentage of ER, PR and HER2 positive was higher than our study.

In the present study, in LVD group 84.6 % patients had left breast and 15.4% had right breast involved. In no LVD group 62% in no LVD group had left breast and 38% had right breast involvement. In Hyun J Y et al[22] (2016) 67% in LVD group and 66.8% in no LVD group left breast was involved; and there was no difference between right or left breast involvement on LV function. As left sided radiotherapy is associated with LVD, in LVD group 53.8% patients received radiotherapy and 85.7% were had received radiotherapy for left breast. Similar results was seen in valentine walker et al study[31].

In the present study, 69% patients in LVD group and 63% in no LVD group received doxorubicin, 77% patients in LVD group and 65.3% in no LVD group received cyclophosphamide, 31% patients in LVD group and 40% in no LVD group received trastuzumab; and 46.2% patients in LVD group and 32% in no LVD group received paclitaxel. In Hyun J Y et al study, 33% patients in LVD and 21.7% in no LVD group received Doxorubicin, 37.8% in LVD and 46% in no LVD group received Epirubicin, 52.4% in LVD group and 58% in no LVD group received cyclophosphamide, 34% in LVD group and 23.5% in no LVD group received paclitaxel, 41.7% in LVD group and 13% in no LVD group received trastuzumab. In Anita Boyd et al study 76% received Doxorubicin and 24% received epirubicin.

At present, anthracyclines (epirubicin, doxorubicin, daunorubicin, idarubicin) and taxanes (paclitaxel) are the two major classes of drugs for breast cancer treatment. Anthracyclines are the most commonly used and out of Anthracyclines, doxorubicin and epirubicin are the most commonly used drugs in clinical practice. Cardio toxicity of Anthracycline is a prominent risk leading to morbidity. The total cumulative dose of anthracyclines is the most significant risk factor for cardiac dysfunction. Cardiac side effects of anthracyclines are dose dependent, for instance doxorubicin[14] is associated with 5% incidence of congestive heart failure when cumulative lifetime dose is 400 mg/$m^2$ is reached, and higher dose leads to exponential increase in risk up to 48% at 700 mg/$m^2$. Therefore it is recommended that cumulative dose of doxorubicin should not exceed 400 mg/$m^2$, and for epirubicin 900 mg/$m^2$.[7]

Cyclophosphamide cardio toxicity is rare and primarily seen in patients receiving high dose (>140mg/kg) before bone marrow transplantation. In breast cancer it never reach to this much high dose. With Trastuzumab, risk of cardiac dysfunction and HF were 5.1 and 1.8% respectively. Docetaxel is frequently used in combination with anthracyclines, cyclophphamide and trastuzumab, also increase the incidence of HF but contribution of individual drug is difficult to assess.

Anthracycline cardio toxicity may be acute, early onset and or late onset. Acute toxicity develops during or within 14 days from end of treatment, which include predominately supraventricular arrhythmia, transient LV dysfunction and ECG changes, develop in <1% of the patients immediately after infusion and is usually reversible. Early onset occur within one year of the treatment, while late onset manifest themselves after several years (median 7 years after treatment).[9] Further, cardio toxicity can be divided into type 1 and type 2. Type 1, is usually caused by anthracyclines by direct myocardial damage by through necrosis or apoptosis of cardiomyocytes caused by cumulative dose and is irreversible. While type 2 cardio toxicity is myocardial

dysfunction rather than cell death not associated with cumulative dose and therefore usually reversible, commonly occurs with trastuzumab.[10]

Cumulative dose of doxorubicin in LVD group was 301 mg/$m^2$and in no LVD group 367 mg/$m^2$, for cyclophosphamide cumulative dose in LVD group was 3034 and in no LVD group 3676, for Trastuzumab cumulative dose in LVD group was 1487 and in no LVD group 2771, for paclitaxel cumulative dose in LVD group was 1383 and in no LVD group 1215. In Hyun J Y et al study cumulative dose of doxorubicin in LVD group 340 and in no LVD group 356, epirubicin in LVD group 108 and no LVD group 135, cyclophosphamide in LVD group 1036 and in no LVD group 1403, paclitaxel in LVD group 1036 and in no LVD group 1403. No patients in our study reached the cumulative dose of doxorubicin to 400mg/$m^2$. Our results were similar to Hyun J Y et al study in which cumulative dose of chemotherapy drugs were lower in LVD group as compared to no LVD group.

Mean Ejection Fraction in LVD group at base line was 61.9%, at mid of chemotherapy it was 49%, at end of chemotherapy it was 43.4% and on follow up echo it was 53.2%. In no LVD group there was no difference in ejection at base line from follow up echocardiography 61% at baseline, during mid of the chemotherapy 61.8 and on third echo 62%. The result of this study is concordance with Hyun J Y et al[22](2016) in which among LVD group baseline mean Ejection Fraction was 64±6.3% and on follow up echocardiography at end of chemotherapy it was 53.9±6.1%.While in no LVD group baseline EF was 68.4% and on follow up echo it was 64%. GLS in LVD group at base line echocardiography was -19.18 ,at mid of chemotherapy it was -15.83, at end of chemotherapy it was -14.46 and on follow up echo it was -17.57( normal= -15.9-to -22.1%).

In our study, GLS in LVD group was -19.1% at baseline echo which was reduced to -15.8 on second echocardiography, -14.4 on third echocardiography and -17.5% on fourth echocardiography. While GLS in no LVD group at baseline was -18.7, and on follow up echo it was -

17.8 and -19.8 on second and third echocardiography respectively. Thus there was linear relationship between Ejection fraction and GLS. In Anita Boyd et al[20](2017) echo done before and 7 days after treatment showed 21% had subclinical dysfunction and GLS was significantly reduced from -20±1.6% to -19.1±1.8%; and no risk factors or clinical parameter was associated with subclinical LV dysfunction. However, in our study GLS was reduced from -19.8 to -17.5 and it was associated with clinical LV dysfunction. In Anita Boyd et al study subclinical LVD was defines as in relative decrease GLS > 11% from baseline while in our study it was defined as > 15% relative percentage reduction from baseline. In literature the combination of high sensitivity troponin with GLS provide greatest sensitivity of 93% and negative predictive value of 91% to predict future cardio toxicity.

The LVEDV in LVD group was 47 mm, in second echo it was 48.8, in third 48.6 and 49 mm in fourth echocardiography. LAVI was 34.3 ml/$m^2$ baseline echocardiography, 33.4 in second echocardiography, 34.6 in third echo and 33.7 in fourth echo. In Hyun J Y et al study LVEDV in LVD group was 47.3 and on follow up echocardiography it was same 47.3 mm. LAVI in LVD group at baseline was 26 and 26.5 ml/$m^2$ on follow up echo. In Anita Boyd et al study LVEDV was 53 at baseline and 54 on follow up echocardiography. So result of our study was similar to results of Hyun et al and Anita et al study in which there is no change in LVEDV and LAVI.

Patient who developed LV dysfunction were immediately informed to treating oncologist and chemotherapy was modified accordingly. Patients were started on heart failure medication. All patient was prescribed RAS inhibitors and B blockers which was up titrated to maximal tolerated dose. 92.3%.9 2.3% patients were in NYHA class 1 and 7.6% who was in NYHA class IV, was prescribed diuretic and MRA in addition to RAS inhibitors and B Blockers. In Hyun J Y et al[22](2016) study symptomatic heart failure developed in 71%.

On follow up echocardiography after 3 months of chemotherapy, 77% patients completely recovered while 23% patients were partially recovered and had mild LV dysfunction. In Hyun J Y et al study after 12 months of follow up 64.6% patients improved where as 35.4% were not recovered.

Patients who were completely recovered, 90% patients were in NYHA class 1 and 10% patient was in NYHA class IV; 40% patients received radiotherapy, 80% patients having Left breast and 20% having right breast involvement. Patient who were partially recovered were 23%, out of which 66.6% patients received radiotherapy and 100 % patients had left breast involved; 66.6% patients received doxorubicin, 66.6% patients received cyclophosphamide, no patients received trastuzumab and 66.6% patients received paclitaxel.

Mean age in complete recovery group was 58 years while in partial recovery group it was 49.6 years. Mean haemoglobin in complete recovery was 10.8 while in partial recovery it was 11g/dl. Mean albumin was 3.93 in complete recovery group vs 3.99 g/dL partial recovery group. Mean BMI was higher in complete recovery i.e. 31.49 vs 23.83 in partial recovery group. Mean BSA was 1.63 in complete recovery group vs 1.68 in partial recovery group. Mean radiotherapy dose was 50.16 in complete recovery group and 46 Gy partial recovery group. In partial recovery group, 66.6% patients were in cancer stage III and 33.3% in stage IV. In partial recovery group, 33.3% patient was as ER and HER2 positive while no patients were PR positive. 10% patients in complete recovery and 33.3% in partial recovery was hypertensive. Except paclitaxel mean doses of chemotherapy was also lower in partial recovery group. 33.3% patient received no radiotherapy, 33.3% received 40 Gy and 33.3% patient received 52 Gy. In Hyun J Y et al mean dose of paclitaxel was higher in LVD group while doxorubicin and cyclophosphamide dose was less.

In our study predictors of LV dysfunction was found to be essential hypertension, left breast involvement, high BMI and high dose of

radiotherapy, although it was statistically non-significant (p>0.005). ER positive, PR positive and HER2 positive patients are also at risk of developing LVD. Higher cancer stage i.e. stage III and IV are more prone for LV dysfunction. The mean doses of chemotherapy was lower in LVD group as compared to no LVD group. There was no difference in age, haemoglobin, albumin or BSA between the two groups. While in Hyun J Y et al study predictors of LVD was low BMI, advanced age and trastuzumab therapy; and cumulative doses of doxorubicin, cyclophosphamide and of radiotherapy were lower LVD group as compared to no LVD group. In Anita Boyd et al study no risk factors or clinical parameters were associated with development of subclinical LV dysfunction.

Predictors of partial recovery in our study were cancer stage III-IV, Low age, low BMI, low dose of radiotherapy, low dose of mean dose of chemotherapy except Paclitaxel and Left breast involvement. While haemoglobin, albumin and BSA are not related to recovery of LV function.

There were several limitations of the present study. First the present we included a breast cancer patients who came to single canter limiting generalizability to other population. Second is the small sample size. Third is that present study included both early and advanced stage of breast cancer. Patients with advanced stage receive more cycles of chemotherapy and radiotherapy that would affect the incidence of CTRCD. Fourth was duration of study was short. Fifth, coronary angiography was not performed in LVD group; thus, possibility of CAD cannot be excluded. Sixth, the biomarkers such as troponin and BNP are not routinely performed and laboratory investigations like lipid profile, blood glucose were not included in our study. Seventh, sick patients with advanced disease was not included.

In conclusion, despite these limitations, the results of the present study demonstrated that incidence of acute card toxicity is significant and essential hypertension, left breast involvement, high dose of

radiotherapy, high BMI and advance cancer stage were independent predictors of LV dysfunction. Therefore, development of CTRCD should be carefully monitored in patients with breast cancer who are obese, left breast involved, hypertensive and those receiving high dose of radiotherapy. The present study also concluded that early diagnosis, prompt initiation of HF therapy with modification of chemotherapy, in more than two third of patients LVD can be recovered. Whereas advanced cancer stage, low BMI, left breast involvement and patient receiving paclitaxel has lower chance of recovery.

# LIMITATIONS

Patients who came to single canter were included in the present study thus limiting generalizability to other population.

The sample size was small i.e. 97 patients.

Present study included both early and advanced stage of breast cancer. Patients with advanced stage receive more cycles of chemotherapy and radiotherapy that would affect the incidence of CTRCD.

Duration of study was short. Patients were followed up only during the chemotherapy period.

Coronary angiography was not performed in LVD group; thus, possibility of CAD cannot be excluded.

The biomarkers such as troponin and BNP are not routinely performed and laboratory investigations like lipid profile, blood glucose were not included in our study.

Sick patients with advanced disease were not included.

# SUMMARY AND CONCLUSION

- Chemotherapeutics related cardiac dysfunction (CTRCD) was evaluated in the present study using 2 D echocardiography and global longitudinal strain.
- Total 97 newly diagnosed breast cancer patients who came to oncology wing were enrolled and LV function using echocardiography and global longitudinal strain before starting chemotherapy and then, serial follow up at mid of chemotherapy and at the end of chemotherapy was done.
- Incidence of acute cardiac toxicity in the present study was 13.4%.
- In our study predictors of LV dysfunction was found to be essential hypertension, left breast involvement, high BMI and high dose of radiotherapy although it was statistically non-significant. ER positive, PR positive and HER2 positive patients are also at risk of developing LVD. Higher cancer stage i.e. stage III and IV are more prone for LV dysfunction.
- LV dysfunction was independent of cumulative doses of chemotherapy.
- 77% patients were completely recovered following modification of chemotherapy and initiation of heart failure therapy.
- 23% patient were partially recovered.
- Cancer stage III-IV, Low age, low BMI, low dose of radiotherapy, low dose of mean dose of chemotherapy except Paclitaxel and Left breast involvement are markers for partial recovery.

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# PROFORMA

Enrolment date: ---------- Sr. No. ----------

Name: ---------- Age: ----------

Adm No. : ---------- Address: ----------

Occupation: ---------- phone no. ----------

Diagnosis: ---------- Stage: ----------

P/H/O of RT/CT/Surgery ----------

Type of Chemotherapy: ----------

ECOG performance status: ----------

Physical Examination:

Height: ---------- BSA: ----------

Weight: ---------- BMI: ----------

Systolic BP: ---------- Diastolic BP: ----------

Pallor: ------ Icterus: ---------- Cyanosis: -------- Edema: ---------

JVP: -------- Ascites: ---------- LAP: ----------

Signature of Candidate

Signature of Supervisor

**CVS Examination:** ----------

| | Positive findings | |
|---|---|---|
| Inspection | | |
| Palpation | | |
| Auscultation | Aortic area | Pulmonary area |
| | Mitral area | Tricuspid area |

**Cardiovascular risk Factors:**

| | |
|---|---|
| Diabetes Mellitus | |
| Hypertension | |
| Smoking | |
| CAD | |
| Obesity | |
| Sedentary life style (MET) | |
| Family h/o CAD | |

**Past History Of:**

| | |
|---|---|
| Valvular Heart Disease | |
| Cardiomyopathy | |
| Ischemic Heart Disease | |
| Arrhythmia | |
| Congestive heart failure | |



Signature of Candidate

Signature of Supervisor

**Base line investigation:**

| | Before chemotherapy | Mid of the chemotherapy | End of the chemotherapy |
|---|---|---|---|
| Chemotherapy and dose | | | |
| Radiotherapy | | | |
| Physical examination | | | |
| NYHA class | | | |
| Systolic BP (mm of Hg) | | | |
| Diastolic BP (mm of Hg) | | | |
| Hemoglobin (g/dl) | | | |
| TLC (per $mm^{3)}$ | | | |
| Platelet (per $mm^{3)}$ | | | |
| RBS (mg/dl) | | | |
| Total Cholesterol (mg/dl) | | | |
| Bilirubin (mg/dl) | | | |
| SGOT (IU/L) | | | |
| SGPT (IU/L) | | | |
| Total protein ( g/dl) | | | |
| Albumin (g/dl) | | | |
| Blood Urea (mg/dl) | | | |
| S creatinine (mg/dl) | | | |
| CXR | | | |
| ECG Changes | | | |

Signature of Candidate

Signature of Supervisor

**ECHOCARDIOGRAPHY**

| | Before chemotherapy | Mid of the chemotherapy | End of the chemotherapy |
|---|---|---|---|
| Aorta root (mm) | | | |
| LA SIZE (s) (mm) | | | |
| LA SIZE (d) (mm) | | | |
| LAVI (s) | | | |
| LAVI (d) | | | |
| LVEDV | | | |
| LVMPI | | | |
| CRS | | | |
| Global Circumferential strain (%) | | | |
| Global longitudinal strain (%) | | | |
| MAPSE | | | |
| PASP | | | |
| E/A | | | |
| E/e' | | | |
| S' | | | |
| e' | | | |
| a' | | | |
| Ejection fraction (%) | | | |
| Global longitudinal strain (%) | | | |
| Longitudinal Strain rate | | | |
| MR (mild/mod/severe) | | | |
| AR (mild/mod/severe) | | | |
| TR (mild/mod/severe) | | | |
| PR (mild/mod/severe) | | | |
| Pericardial effusion | | | |



Signature of Candidate

Signature of Supervisor

**MUGA scan:** ----------

**EASTERN COOPERATIVE ONCOLOGY GROUP (ECOG)** performance status:

| GRADE | PERFORMANCE STATUS |
|---|---|
| 0 | Fully active, able to carry on all pre disease performance without restriction. |
| 1 | Restricted in physical strenuous activity but ambulatory and able to carry out work of a light or sedentary nature e.g. light house hold work, office work. |
| 2 | Ambulatory and capable of all self-care but unable to carry out any work activities; up and about more than 50 % of waking hours. |
| 3 | Capable of only limited self-care; confined to bed or chair more than 50 % of waking hours. |
| 4 | Completely disabled; cannot carry on any self-care; totally confined to bed or chair. |
| 5 | Dead |

Signature of Candidate

Signature of Supervisor

CTRCD: Cancer related cardiac dysfunction

DNA: Deoxyribonucleic acid

LV: left ventricle

CVD: cardio vascular disease

CHF: congestive heart failure

ECOG: eastern cooperative oncology group

LVEF: left ventricle ejection fraction

GLS: global longitudinal strain

IHD: ischemic heart disease

MUGA: multigated acquisition scan

EF: ejection fraction



Signature of Candidate

Signature of Supervisor

| Sr. No | Age | MRD No. | Hemoglobin | Albumin | HTN | SBP | DBP | DM | east involv | BMI | BSA | ER+ | PR+ | HER2+ | Cancer Stage | T | N | M | Surgery | RT dosage Gy | Doxorubicin | Cylophosphamide | Trastuzumab | Carboplatin |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | 56 | 656237 | 11.5 | 4.5 | No | 110 | 60 | No | Right | 26 | 1.56 | Negative | Negative | Positive | II | 3 | 1 | 0 | yes | 30 | - | - | 500 | 2400 |
| 2 | 63 | 869729 | 11.7 | 3.8 | No | 116 | 76 | No | Left | 24.46 | 1.56 | Negative | Negative | Positive | III | 2 | 0 | 0 | yes | No | - | - | 2600 | - |
| 3 | 41 | 911336 | 9.7 | 4.7 | No | 120 | 76 | No | Left | 24.91 | 1.73 | Negative | Negative | Negative | III | 2 | 1 | 0 | yes | 50 | - | - | - | 2450 |
| 4 | 61 | 669852 | 13 | 3.6 | No | 118 | 69 | No | Right | 28.57 | 1.63 | Negative | Negative | Negative | IV | 3 | 1 | 0 | yes | No | 500 | 5000 | - | - |
| 5 | 63 | 222118 | 8.11 | 3.6 | No | 126 | 83 | No | Left | 26.84 | 1.68 | Negative | Negative | Negative | IV | 3 | 2 | 1 | yes | No | - | - | - | - |
| 6 | 34 | 943306 | 9.2 | 3.8 | No | 130 | 70 | No | Left | 28.62 | 1.66 | Negative | Negative | Positive | III | 1 | 1 | 0 | yes | No | 400 | - | 1740 | 2400 |
| 7 | 55 | 933316 | 12.7 | 4.5 | No | 122 | 76 | No | Left | 26.2 | 1.63 | Negative | Negative | positive | X | 3 | 1 | 0 | yes | No | - | - | 3960 | - |
| 8 | 50 | 933177 | 10.8 | 3.3 | No | 130 | 82 | no | Left | 23.5 | 1.59 | Negative | Negative | Positive | III | 3 | 1 | 0 | yes | 30 | - | - | 1320 | 1350 |
| 9 | 67 | 937187 | 12.8 | 3.9 | No | 127 | 74 | No | Left | 25.2 | 1.68 | Negative | Negative | Negative | III | 2 | 3 | 0 | yes | 45 | 360 | 3600 | - | - |
| 10 | 55 | 934985 | 12.4 | 4 | No | 130 | 76 | No | Left | 24.8 | 1.7 | Positive | Positive | Negative | I | 2 | 0 | 0 | yes | No | - | - | - | - |
| 11 | 45 | 308735 | 11.8 | 3.8 | No | 128 | 74 | No | Right | 34.72 | 1.94 | Negative | Negative | Negative | I | 2 | 0 | 0 | yes | 42.5 | 400 | 4000 | - | - |
| 12 | 56 | 955759 | 9.7 | 4.1 | No | 134 | 88 | No | Right | 21.05 | 1.41 | Negative | Negative | Negative | III | 2 | 0 | 0 | yes | 46 | 460 | 4600 | - | - |
| 13 | 46 | 941607 | 12.5 | 3.8 | No | 136 | 80 | No | Right | 29.72 | 1.92 | Negative | Negative | Negative | II | 2 | 0 | 0 | yes | No | 440 | 4400 | - | - |
| 14 | 35 | 953275 | 13.1 | 4.2 | No | 138 | 86 | No | Right | 27.11 | 1.56 | Negative | Negative | Negative | III | 4 | 2 | 0 | yes | 27.5 | 360 | 3600 | - | - |
| 15 | 46 | 388958 | 9.9 | 4.1 | No | 126 | 78 | No | Left | 28.48 | 1.76 | Negative | Negative | Positive | III | 4 | 2 | 0 | yes | No | - | - | 1520 | 2400 |
| 16 | 42 | 405365 | 11.4 | 3.5 | No | 127 | 77 | No | Right | 26 | 1.59 | Negative | Negative | Negative | IV | 2 | 1 | 1 | yes | 55 | 500 | 5000 | - | - |
| 17 | 45 | 480775 | 9.7 | 3.5 | No | 136 | 80 | No | Left | 37.78 | 1.64 | Negative | Negative | Negative | II | 2 | 0 | 0 | yes | 30 | 440 | 4400 | - | - |
| 18 | 53 | 859097 | 10.2 | 4.2 | No | 130 | 88 | No | Left | 26.91 | 1.63 | Negative | Negative | Positive | III | 4 | 1 | 0 | yes | 42.5 | - | 2700 | 880 | - |
| 19 | 64 | 962661 | 10 | 4.4 | No | 130 | 88 | No | Right | 31.72 | 1.58 | Negative | Negative | Negative | II | 2 | 1 | 0 | yes | No | 335 | 3350 | - | - |
| 20 | 55 | 955665 | 11 | 3.9 | No | 128 | 78 | No | Left | 25.8 | 1.72 | Negative | Negative | Negative | II | 2 | 1 | 0 | yes | 42 | 335 | 3350 | - | - |
| 21 | 62 | 970951 | 8.1 | 3.5 | No | 130 | 88 | No | Right | 37.28 | 1.7 | Negative | Negative | Negative | III | 2 | 3 | 0 | yes | 42 | 400 | 4000 | - | - |
| 22 | 33 | 927694 | 8.8 | 3.9 | No | 128 | 70 | No | Right | 25.8 | 1.8 | Negative | Negative | Negative | III | 4 | 2 | 0 | yes | No | 380 | 3000 | - | 1800 |
| 23 | 30 | 934307 | 13.1 | 4.06 | No | 128 | 78 | no | Left | 25.45 | 1.48 | Negative | Negative | Positive | II | 2 | 0 | 0 | yes | No | - | - | 2420 | - |
| 24 | 53 | 930608 | 10.1 | 4.6 | No | 130 | 68 | No | Left | 21.64 | 1.57 | Negative | Negative | Positive | III | 2 | 3 | 0 | yes | 50.4 | 270 | 2700 | 3800 | - |
| 25 | 31 | 776090 | 11.5 | 3.7 | No | 127 | 60 | No | Left | 26.56 | 1.61 | Negative | Negative | Negative | II | 3 | 1 | 0 | yes | 34.7 | 380 | 3800 | - | - |
| 26 | 65 | 971260 | 11.6 | 4 | No | 120 | 68 | No | Left | 28.22 | 1.59 | Negative | Negative | Negative | II | 3 | 0 | 0 | yes | 46 | 380 | 3800 | - | - |
| 27 | 53 | 937614 | 10 | 4.8 | No | 128 | 80 | No | Left | 33.53 | 1.77 | Negative | Negative | Negative | X | 3 | 1 | 0 | yes | No | 400 | 4000 | - | - |
| 28 | 52 | 970558 | 8.2 | 4 | No | 126 | 76 | No | Right | 24.8 | 1.79 | Negative | Negative | Negative | III | 3 | 1 | 0 | yes | No | 405 | 4050 | - | - |
| 29 | 60 | 944390 | 5.8 | 3.8 | No | 132 | 82 | No | Left | 23.5 | 1.6 | Negative | Negative | Negative | II | 2 | 0 | 0 | yes | No | 400 | 4000 | - | - |
| 30 | 50 | 772456 | 10.8 | 4.1 | No | 128 | 83 | No | Right | 24.8 | 1.54 | Negative | Positive | Positive | III | 2 | 3 | 0 | yes | 40 | 360 | 3600 | 2540 | - |
| 31 | 63 | 965930 | 6.5 | 2.01 | No | 134 | 76 | No | Left | 24 | 1.71 | Negative | Negative | Negative | III | 3 | 3 | 0 | yes | No | 440 | 4400 | - | - |
| 32 | 53 | 866338 | 11.4 | 3.4 | No | 128 | 70 | No | Right | 27 | 1.59 | Negative | Positive | Positive | III | 2 | 3 | 0 | yes | 42.5 | 400 | 4000 | 2270 | - |
| 33 | 64 | 979946 | 12.5 | 4.1 | No | 120 | 70 | No | Right | 30.98 | 1.65 | Negative | Negative | Negative | II | 2 | 1 | 0 | yes | No | 400 | 4000 | - | - |
| 34 | 59 | 976901 | 13 | 4.1 | No | 128 | 88 | No | Right | 31.94 | 171 | Negative | Negative | Negative | I | 2 | 0 | 0 | yes | No | 370 | 3700 | - | - |
| 35 | 39 | 40436 | 10.6 | 4.2 | No | 116 | 70 | No | Left | 21.03 | 1.59 | Negative | Negative | Negative | III | 3 | 2 | 0 | yes | 46 | 360 | 3600 | - | - |
| 36 | 33 | 982659 | 8.1 | 3.3 | No | 110 | 67 | No | Left | 14.4 | 1.57 | Negative | Negative | Negative | III | 4 | 3 | 0 | yes | No | 310 | 3100 | - | - |
| 37 | 34 | 988212 | 12.1 | 4.13 | No | 106 | 70 | No | Left | 26 | 1.71 | Negative | Negative | Negative | III | 3 | 0 | 0 | yes | 41.6 | - | 5400 | - | - |
| 38 | 51 | 994935 | 11.2 | 4.1 | No | 110 | 68 | no | Left | 27.11 | 1.56 | Negative | Negative | Negative | II | 3 | 0 | 0 | yes | 50.4 | 360 | 3600 | - | - |
| 39 | 77 | 425488 | 11.1 | 4.1 | No | 112 | 78 | No | Left | 23.7 | 1.57 | Negative | Negative | Negative | III | 2 | 0 | 0 | yes | 40 | - | - | - | 1650 |
| 40 | 45 | 1006735 | 6.6 | 3.6 | No | 128 | 88 | No | Left | 33.79 | 1.84 | Negative | Negative | Negative | II | 2 | 0 | 0 | yes | No | 360 | 3600 | - | - |
| 41 | 38 | 997481 | 12.2 | 4.5 | No | 130 | 76 | No | Left | 32.8 | 1.79 | Negative | Negative | Negative | III | 3 | 3 | 0 | yes | 52.5 | 365 | 4130 | - | 780 |
| 42 | 54 | 1019331 | 12.6 | 3.92 | No | 127 | 68 | No | Left | 31.58 | 1.73 | Negative | Negative | Negative | II | 2 | 0 | 0 | yes | No | 100 | 1000 | - | - |
| 43 | 55 | 966571 | - | - | No | 132 | 88 | No | Left | 28.28 | 1.71 | Negative | Negative | Negative | III | 3 | 3 | 0 | yes | No | 400 | 4000 | - | - |
| 44 | 55 | 806682 | 11.6 | 3.7 | No | 132 | 80 | No | Left | 27.7 | 1.61 | Negative | Negative | Negative | III | 3 | 1 | 0 | yes | 50 | 360 | 3800 | - | 260 |
| 45 | 45 | 1012024 | 10.3 | 3.78 | No | 138 | 70 | No | Left | 25 | 1.68 | Negative | Negative | Negative | II | 3 | 2 | 0 | yes | 50.4 | 440 | 4400 | - | 1120 |
| 46 | 61 | 970851 | 9.7 | 3.4 | No | 128 | 80 | No | Right | 44.15 | 1.9 | Negative | Negative | Negative | III | 1 | 3 | 0 | yes | 50.4 | 400 | 4000 | - | 290 |
| 47 | 55 | 564851 | 10.3 | 4.2 | No | 122 | 68 | No | Left | 35.09 | 1.76 | Negative | Negative | Negative | II | 2 | 2 | 0 | yes | No | 400 | 4000 | - | - |
| 48 | 33 | 1048372 | 10.5 | 4.2 | No | 130 | 76 | No | Right | 31.03 | 1.69 | Negative | Negative | Negative | II | 2 | 1 | 0 | yes | 30.6 | 360 | 3600 | - | - |
| 49 | 59 | 1031146 | 12 | 4.19 | No | 122 | 70 | No | Left | 34.13 | 1.81 | negative | Negative | Negative | III | 2 | 3 | 0 | yes | 42.5 | 400 | 4000 | - | - |
| 50 | 45 | 1070503 | 12.7 | 4.2 | No | 128 | 80 | No | Left | 26.99 | 1.63 | negative | Negative | Positive | II | 3 | 2 | 0 | yes | 30 | - | - | 3580 | 3600 |
| 51 | 49 | 1064089 | 9.8 | 4.4 | No | 132 | 80 | No | Right | 26.5 | 1.71 | Negative | Negative | Negative | III | 2 | 1 | 0 | yes | 42.5 | 510 | 5100 | - | - |
| 52 | 42 | 861342 | 12.1 | 4.8 | No | 126 | 70 | No | Left | 28 | 1.78 | Negative | Negative | Positive | III | 3 | 2 | 0 | yes | 50.4 | - | - | 3380 | 3600 |
| 53 | 48 | 806682 | 11.6 | 3.7 | No | 132 | 84 | No | Right | 27.8 | 1.61 | Negative | Negative | Negative | II | 2 | 1 | 0 | yes | 50 | - | - | - | - |
| 54 | 52 | 1083876 | 8.5 | 4.1 | No | 128 | 78 | No | Left | 27 | 1.78 | Negative | Negative | Negative | I | 1 | 0 | 0 | yes | 42 | 100 | 1000 | - | - |
| 55 | 39 | 1098001 | 8.8 | 3.7 | No | 132 | 78 | No | Left | 24.6 | 1.68 | Negative | Positive | Positive | II | 2 | 0 | 0 | yes | No | 360 | 3600 | 2740 | - |
| 56 | 60 | 1010449 | 11 | 4.1 | No | 120 | 70 | No | right | 23.8 | 1.58 | Negative | Negative | Negative | II | 2 | 2 | 0 | yes | No | 405 | 4050 | - | - |
| 57 | 50 | 1048259 | 10.8 | 4.3 | No | 134 | 80 | No | Left | 26 | 1.71 | Negative | Negative | Negative | III | 2 | 2 | 0 | yes | No | 380 | 3800 | - | - |
| 58 | 53 | 1016643 | 12.9 | 4.5 | No | 126 | 70 | No | Left | 28 | 1.72 | Negative | Negative | Positive | III | 3 | 2 | 0 | yes | 50 | - | - | 3380 | 3600 |

| Sr. No | Age | MRD No. | Paclitaxel | Docetaxel | NYHA Class | BNP | Echo | LAVI | Aortic Root | LVID (S) | LVID (D) | IVST (S) | IVST(D) | LVPW(S) | LVPW(D) | EF(%) | Mild LVD | Moderate LVD | Severe LVD | GLS(%) | GCS (%) | MAPSE | DT(ms) | e'(cm/s) | s'(cm/s) | E/e' | DD1 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | 56 | 656237 | - | - | - | - | 1st | 35 | 25 | 34 | 48 | 9 | 8 | 9 | 6 | 58 | NO | NO | NO | -20 | -22 | 12 | 160 | 10 | 10 | 10 | NO |
| 2 | 63 | 869729 | - | - | - | - | 1st | 36 | 25 | 34 | 48 | 9 | 6 | 9 | 7 | 58 | NO | NO | NO | -20 | -22 | 12 | 210 | 10 | 10 | 4 | NO |
| 3 | 41 | 911336 | - | - | - | - | 1st | 36 | 25 | 34 | 48 | 10 | 8 | 9 | 6 | 63 | NO | NO | NO | -20.1 | -22 | 12 | 210 | 12 | 12 | 6 | NO |
| 4 | 61 | 669852 | - | - | - | - | 1st | 35 | 26 | 30 | 46 | 10 | 7 | 9 | 6 | 60 | NO | NO | NO | -20 | -22 | 12 | 210 | 10 | 11 | 10 | NO |
| 5 | 63 | 222118 | 400 | - | - | - | 1st | 30 | 22 | 34 | 46 | 10 | 7 | 9 | 6 | 60 | NO | NO | NO | -19 | -26 | 12 | 198 | 12 | 10 | 6 | NO |
| 6 | 34 | 943306 | - | - | - | - | 1st | 22 | 25 | 34 | 46 | 10 | 8 | 9 | 8 | 60 | NO | NO | NO | -20 | -19 | 12 | 180 | 8 | 12 | 6 | NO |
| 7 | 55 | 933316 | 1200 | - | - | - | 1st | 38 | 25 | 30 | 40 | 11 | 10 | 11 | 10 | 65 | NO | NO | NO | -22 | -20 | 13 | 189 | 9.5 | 12 | 14 | yes |
| 8 | 50 | 933177 | - | - | - | - | 1st | 28 | 30 | 30 | 46 | 9 | 6 | 9 | 6 | 62 | NO | NO | NO | -19 | -23 | 12 | 190 | 10 | 12 | 6 | NO |
| 9 | 67 | 937187 | - | - | - | - | 1st | 28 | 24 | 34 | 46 | 9 | 8 | 9 | 8 | 60 | NO | NO | NO | -20 | -23 | 13 | 200 | 11 | 12 | 4 | NO |
| 10 | 55 | 934985 | - | - | - | - | 1st | 36 | 25 | 30 | 45 | 10 | 9 | 9 | 8 | 60 | NO | NO | NO | -19 | -24.2 | 15 | 198 | 11 | 12 | 9 | NO |
| 11 | 45 | 308735 | - | - | - | - | 1st | 26 | 24 | 32 | 42 | 10 | 9 | 10 | 9 | 62 | NO | NO | NO | -19.8 | -20 | 12 | 180 | 10 | 12 | 8 | NO |
| 12 | 56 | 955759 | - | - | - | - | 1st | 29 | 25 | 32 | 46 | 10 | 9 | 9 | 8 | 62 | NO | NO | NO | -19.1 | -20 | 13 | 200 | 10 | 12 | 6 | NO |
| 13 | 46 | 941607 | - | - | - | - | 1st | 35 | 27 | 30 | 46 | 9 | 8 | 9 | 6 | 60 | NO | NO | NO | -18 | -21 | 12 | 198 | 10 | 12 | 4 | NO |
| 14 | 35 | 953275 | 1040 | - | - | - | 1st | 35 | 25 | 32 | 45 | 9 | 6 | 10 | 7 | 58 | NO | NO | NO | -19.8 | -22 | 12 | 190 | 10 | 10 | 6 | NO |
| 15 | 46 | 388958 | - | - | - | - | 1st | 32 | 26 | 30 | 46 | 9 | 6 | 9 | 7 | 60 | NO | NO | NO | -19 | -22 | 12 | 220 | 10 | 12 | 6 | NO |
| 16 | 42 | 405365 | 260 | - | - | - | 1st | 37 | 26 | 35 | 47 | 9 | 6 | 9 | 6 | 62 | NO | NO | NO | -18.5 | -24 | 14 | 198 | 10 | 12 | 6 | NO |
| 17 | 45 | 480775 | - | - | - | - | 1st | 37 | 26 | 35 | 47 | 9 | 6 | 9 | 6 | 62 | NO | NO | NO | -18.5 | -24 | 14 | 198 | 10 | 12 | 6 | NO |
| 18 | 53 | 859097 | - | - | - | - | 1st | 33 | 26 | 34 | 48 | 10 | 6 | 10 | 9 | 62 | NO | NO | NO | -19 | -24 | 14 | 210 | 10 | 12 | 6 | NO |
| 19 | 64 | 962661 | - | - | - | - | 1st | 35 | 26 | 34 | 47 | 9 | 6 | 9 | 6 | 60 | NO | NO | NO | -19.2 | -20.4 | 15 | 210 | 10 | 12 | 6 | NO |
| 20 | 55 | 955665 | - | - | - | - | 1st | 34 | 26 | 35 | 46 | 9 | 7 | 9 | 6 | 60 | NO | NO | NO | -20.2 | -22.8 | 12 | 210 | 10 | 12 | 4 | NO |
| 21 | 62 | 970951 | 1500 | - | - | - | 1st | 35 | 28 | 35 | 48 | 9 | 6 | 9 | 6 | 62 | NO | NO | NO | -19.4 | -22.4 | 12 | 200 | 10 | 12 | 4 | NO |
| 22 | 33 | 927694 | 1200 | - | - | - | 1st | 34 | 27 | 35 | 47 | 10 | 7 | 10 | 8 | 58 | NO | NO | NO | -18.9 | -24 | 12 | 200 | 10 | 12 | 4 | NO |
| 23 | 30 | 934307 | 2750 | - | - | - | 1st | 35 | 24 | 34 | 48 | 9 | 6 | 9 | 7 | 62 | NO | NO | NO | -18 | -25 | 12 | 210 | 10 | 12 | 4 | NO |
| 24 | 53 | 930608 | 1040 | - | - | - | 1st | 35 | 26 | 34 | 46 | 9 | 6 | 9 | 7 | 62 | NO | NO | NO | -18.6 | -26 | 12 | 200 | 11 | 12 | 2 | NO |
| 25 | 31 | 776090 | - | - | - | - | 1st | 36 | 24 | 34 | 45 | 10 | 8 | 9 | 6 | 60 | NO | NO | NO | -17.8 | -25 | 12 | 190 | 11 | 12 | 2 | NO |
| 26 | 65 | 971260 | - | - | - | - | 1st | 35 | 26 | 35 | 48 | 9 | 6 | 9 | 7 | 60 | NO | NO | NO | -18 | -22.4 | 13 | 200 | 11 | 12 | 4 | NO |
| 27 | 53 | 937614 | - | - | - | - | 1st | 32 | 24 | 34 | 45 | 9 | 7 | 9 | 8 | 60 | NO | NO | NO | -18.6 | -20 | 15 | 200 | 10 | 14 | 4 | NO |
| 28 | 52 | 970558 | - | - | - | - | 1st | 34 | 26 | 34 | 47 | 9 | 6 | 9 | 6 | 62 | NO | NO | NO | -19.2 | -20.2 | 14 | 200 | 12 | 14 | 6 | NO |
| 29 | 60 | 944390 | - | - | - | - | 1st | 35 | 25 | 34 | 45 | 10 | 9 | 9 | 7 | 56 | NO | NO | NO | -21 | -22.9 | 15 | 220 | 12 | 15 | 4 | NO |
| 30 | 50 | 772456 | 1078 | - | - | - | 1st | 34 | 28 | 35 | 46 | 9 | 6 | 9 | 7 | 58 | NO | NO | NO | -19 | -22 | 12 | 190 | 10 | 12 | 2 | NO |
| 31 | 63 | 965930 | 900 | - | - | - | 1st | 32 | 26 | 35 | 46 | 9 | 7 | 9 | 6 | 58 | NO | NO | NO | -20.3 | -23 | 15 | 210 | 15 | 10 | 2 | NO |
| 32 | 53 | 866338 | 1650 | - | - | - | 1st | 34 | 28 | 34 | 46 | 9 | 7 | 9 | 6 | 58 | NO | NO | NO | -19 | -24 | 12 | 220 | 10 | 12 | 2 | NO |
| 33 | 64 | 979946 | 1040 | - | - | - | 1st | 34 | 28 | 35 | 46 | 10 | 8 | 9 | 7 | 60 | NO | NO | NO | -15 | -20 | 12 | 190 | 10 | 12 | 4 | NO |
| 34 | 59 | 976901 | - | - | - | - | 1st | 34 | 24 | 35 | 45 | 9 | 6 | 9 | 7 | 60 | NO | NO | NO | -16 | -20 | 12 | 200 | 10 | 12 | 2 | NO |
| 35 | 39 | 40436 | 800 | - | - | - | 1st | 32 | 22 | 35 | 45 | 9 | 7 | 9 | 7 | 62 | NO | NO | NO | -19.8 | -23 | 12 | 200 | 11 | 12 | 4 | NO |
| 36 | 33 | 982659 | 400 | - | - | - | 1st | 34 | 28 | 34 | 48 | 9 | 6 | 9 | 6 | 62 | NO | NO | NO | -18 | -22 | 12 | 210 | 10 | 11 | 4 | NO |
| 37 | 34 | 988212 | - | - | - | - | 1st | 34 | 24 | 36 | 48 | 10 | 7 | 9 | 6 | 62 | NO | NO | NO | -19.4 | -22 | 14 | 196 | 10 | 12 | 4 | NO |
| 38 | 51 | 994935 | 1100 | - | - | - | 1st | 34 | 28 | 39 | 48 | 10 | 9 | 10 | 8 | 62 | NO | NO | NO | -20 | -25 | 14 | 200 | 10 | 12 | 4 | NO |
| 39 | 77 | 425488 | 1650 | - | - | - | 1st | 43 | 20 | 29 | 46 | 13 | 12 | 13 | 12 | 60 | NO | No | NO | -18 | -20 | 11 | 200 | 10 | 11 | 18.5 | NO |
| 40 | 45 | 1006735 | - | - | - | - | 1st | 35 | 26 | 35 | 49 | 9 | 6 | 10 | 7 | 60 | NO | NO | NO | -18.2 | -25 | 12 | 200 | 9 | 12 | 4 | NO |
| 41 | 38 | 997481 | - | - | - | - | 1st | 35 | 26 | 38 | 45 | 10 | 9 | 9 | 7 | 62 | NO | NO | NO | -18.8 | -24.2 | 12 | 200 | 9 | 12 | 2 | NO |
| 42 | 54 | 1019331 | - | - | - | - | 1st | 35 | 26 | 34 | 48 | 9 | 6 | 9 | 7 | 62 | NO | NO | NO | -18.8 | -22.8 | 12 | 210 | 10 | 12 | 2 | NO |
| 43 | 55 | 966571 | - | - | - | - | 1st | 36 | 24 | 34 | 50 | 9 | 6 | 9 | 6 | 60 | NO | NO | NO | -17.2 | -20 | 12 | 200 | 9 | 10 | 7 | NO |
| 44 | 55 | 806682 | - | - | - | - | 1st | 34 | 25 | 35 | 48 | 9 | 6 | 9 | 7 | 62 | NO | NO | NO | -19.2 | -24 | 12 | 200 | 10 | 12 | 4 | NO |
| 45 | 45 | 1012024 | - | - | - | - | 1st | 34 | 24 | 35 | 48 | 9 | 6 | 9 | 6 | 62 | NO | NO | NO | -19.4 | -24.3 | 12 | 200 | 10 | 12 | 4 | NO |
| 46 | 61 | 970851 | - | - | - | - | 1st | 34 | 22 | 35 | 48 | 9 | 6 | 9 | 6 | 60 | NO | NO | NO | -17.8 | -24 | 12 | 10 | 10 | 12 | 4 | NO |
| 47 | 55 | 564851 | 920 | - | - | - | 1st | 34 | 24 | 35 | 48 | 9 | 6 | 9 | 6 | 62 | NO | NO | NO | -19.4 | -24.3 | 12 | 200 | 10 | 12 | 4 | NO |
| 48 | 33 | 1048372 | - | - | - | - | 1st | 34 | 24 | 35 | 48 | 9 | 6 | 9 | 6 | 60 | NO | NO | NO | -19 | -22 | 12 | 200 | 10 | 12 | 4 | NO |
| 49 | 59 | 1031146 | - | - | - | - | 1st | 38 | 24 | 34 | 48 | 9 | 6 | 9 | 6 | 60 | NO | NO | NO | -18.4 | -21.9 | 12 | 196 | 11 | 12 | 2 | NO |
| 50 | 45 | 1070503 | - | - | - | - | 1st | 34 | 25 | 34 | 48 | 10 | 9 | 10 | 8 | 62 | NO | NO | NO | -17.8 | -21.9 | 12 | 180 | 10 | 12 | 2 | NO |
| 51 | 49 | 1064089 | - | - | - | - | 1st | 34 | 22 | 28 | 40 | 9 | 6 | 9 | 7 | 62 | NO | NO | NO | -19.4 | -22.7 | 12 | 210 | 12 | 10 | 4 | NO |
| 52 | 42 | 861342 | - | - | - | - | 1st | 34 | 23 | 34 | 49 | 9 | 6 | 9 | 6 | 62 | NO | NO | NO | -20.2 | -24.1 | 12 | 200 | 11 | 12 | 2 | NO |
| 53 | 48 | 806682 | 740 | - | - | - | 1st | 34 | 28 | 35 | 43 | 9 | 6 | 9 | 6 | 62 | NO | NO | NO | -18.9 | -24.2 | 12 | 188 | 10 | 12 | 4 | NO |
| 54 | 52 | 1083876 | 1440 | - | - | - | 1st | 34 | 26 | 34 | 47 | 9 | 6 | 9 | 6 | 62 | NO | NO | NO | -18.4 | -22.4 | 12 | 188 | 12 | 12 | 4 | NO |
| 55 | 39 | 1098001 | 1040 | - | - | - | 1st | 34 | 22 | 35 | 48 | 9 | 6 | 9 | 6 | 62 | NO | NO | NO | -18.6 | -24.5 | 12 | 210 | 11 | 12 | 2 | NO |
| 56 | 60 | 1010449 | - | - | - | - | 1st | 34 | 22 | 35 | 48 | 9 | 6 | 9 | 6 | 62 | NO | NO | NO | -17.8 | -22.8 | 12 | 210 | 12 | 11 | 4 | NO |
| 57 | 50 | 1048259 | - | - | - | - | 1st | 34 | 28 | 35 | 48 | 9 | 6 | 9 | 7 | 62 | NO | NO | NO | -18.4 | -22.8 | 12 | 200 | 11 | 12 | 4 | NO |
| 58 | 53 | 1016643 | - | - | - | - | 1st | 34 | 28 | 35 | 48 | 9 | 6 | 9 | 7 | 62 | NO | NO | NO | -18.4 | -22.8 | 12 | 200 | 11 | 12 | 4 | NO |

| Sr. No | Age | MRD No. | DD2 | DD3 | PASP | LAVI | Aortic Root | LVID (S) | LVID (D) | IVST (S) | IVST(D) | LVPW(S) | LVPW(D) | EF(%) | mild LVD | Moderate LVD | Severe LVD | GLS(%) | GCS (%) | MAPSE | DT(ms) | e'(cm/s) | s'(cm/s) | E/e' | DD1 | DD2 | DD3 | PASP | LAVI | Aortic Root |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | 56 | 656237 | NO | NO | 0 | 36 | 26 | 34 | 46 | 9 | 8 | 10 | 7 | 56 | NO | NO | NO | -19 | -20 | 13 | 180 | 12 | 11 | 9 | NO | NO | NO | 0 | 35 | 27 |
| 2 | 63 | 869729 | NO | NO | 0 | 35 | 28 | 35 | 47 | 9 | 7 | 9 | 7 | 60 | NO | NO | NO | -19 | -19 | 12 | 220 | 12 | 11 | 8 | NO | NO | NO | 0 | 36 | 26 |
| 3 | 41 | 911336 | NO | NO | 16 | 35 | 25 | 34 | 47 | 9 | 7 | 9 | 7 | 63 | NO | NO | NO | -19.3 | -23 | 11 | 222 | 11 | 11 | 7 | NO | NO | NO | 16 | 35 | 28 |
| 4 | 61 | 669852 | NO | NO | 0 | 36 | 29 | 33 | 47 | 9 | 8 | 9 | 7 | 62 | NO | NO | NO | -19.8 | -23 | 13 | 222 | 11 | 12 | 8 | NO | NO | NO | 0 | 35 | 28 |
| 5 | 63 | 222118 | NO | NO | 0 | 32 | 24 | 35 | 47 | 9 | 8 | 10 | 7 | 62 | NO | NO | NO | -19.6 | -26 | 12 | 190 | 13 | 10 | 5 | NO | NO | NO | 0 | 32 | 25 |
| 6 | 34 | 943306 | NO | NO | 0 | 26 | 26 | 35 | 47 | 10 | 7 | 9 | 7 | 60 | NO | NO | NO | -20.8 | -19.6 | 11 | 186 | 10 | 12 | 4 | NO | NO | NO | 12 | 30 | 25 |
| 7 | 55 | 933316 | NO | NO | 23 | 39 | 26 | 31 | 48 | 11 | 10 | 11 | 10 | 62 | NO | NO | NO | -21 | -19 | 12 | 200 | 9.8 | 11 | 13.4 | yes | NO | NO | 22 | 38 | 26 |
| 8 | 50 | 933177 | NO | NO | 0 | 30 | 28 | 34 | 47 | 9 | 6 | 9 | 6 | 63 | NO | NO | NO | -19.6 | -22.8 | 12 | 200 | 10 | 12 | 4 | NO | NO | NO | 0 | 32 | 27 |
| 9 | 67 | 937187 | NO | NO | 0 | 30 | 26 | 32 | 47 | 9 | 8 | 10 | 9 | 61 | NO | NO | NO | -19 | -22 | 12 | 210 | 12 | 10 | 6 | NO | NO | NO | 0 | 32 | 25 |
| 10 | 55 | 934985 | NO | NO | 0 | 35 | 26 | 32 | 38 | 10 | 8 | 9 | 8 | 62 | NO | NO | NO | -18.8 | -22 | 12 | 200 | 10 | 12 | 10 | NO | NO | NO | 0 | 37 | 26 |
| 11 | 45 | 308735 | NO | NO | 0 | 28 | 25 | 30 | 45 | 10 | 9 | 9 | 8 | 64 | NO | NO | NO | 19.2 | -20.6 | 10 | 196 | 11 | 13 | 6 | NO | NO | NO | 0 | 30 | 28 |
| 12 | 56 | 955759 | NO | NO | 0 | 35 | 26 | 30 | 48 | 10 | 9 | 9 | 8 | 63 | NO | NO | NO | -19.8 | -20.9 | 14 | 210 | 11 | 13 | 4 | NO | NO | NO | 0 | 34 | 24 |
| 13 | 46 | 941607 | NO | NO | 0 | 36 | 26 | 32 | 47 | 9 | 7 | 9 | 7 | 62 | NO | NO | NO | -18.4 | -21.2 | 11 | 198 | 11 | 12 | 6 | NO | NO | NO | 0 | 35 | 27 |
| 14 | 35 | 953275 | NO | NO | 0 | 36 | 26 | 30 | 46 | 9 | 6 | 10 | 7 | 60 | NO | NO | NO | -21 | -22.8 | 13 | 198 | 11 | 11 | 5 | NO | NO | NO | 0 | 35 | 26 |
| 15 | 46 | 388958 | NO | NO | 0 | 34 | 27 | 32 | 47 | 9 | 7 | 9 | 6 | 62 | NO | NO | NO | -19.5 | -22.4 | 13 | 200 | 10 | 12 | 4 | NO | NO | NO | 0 | 35 | 26 |
| 16 | 42 | 405365 | NO | NO | 0 | 36 | 27 | 34 | 48 | 9 | 7 | 9 | 6 | 64 | NO | NO | NO | -18.8 | -23.8 | 12 | 200 | 11 | 11 | 4 | NO | NO | NO | 0 | 36 | 26 |
| 17 | 45 | 480775 | NO | NO | 0 | 36 | 27 | 34 | 48 | 9 | 7 | 9 | 6 | 64 | NO | NO | NO | -18.8 | -23.8 | 12 | 200 | 11 | 11 | 4 | NO | NO | NO | 0 | 36 | 26 |
| 18 | 53 | 859097 | NO | NO | 0 | 35 | 25 | 34 | 45 | 10 | 6 | 10 | 9 | 65 | NO | NO | NO | -19.8 | -24.3 | 15 | 210 | 11 | 10 | 4 | NO | NO | NO | 0 | 36 | 25 |
| 19 | 64 | 962661 | NO | NO | 15 | 36 | 25 | 35 | 46 | 9 | 7 | 9 | 7 | 60 | NO | NO | NO | -19 | -20.8 | 14 | 216 | 11 | 10 | 4 | NO | NO | NO | 12 | 35 | 24 |
| 20 | 55 | 955665 | NO | NO | 25 | 34 | 27 | 35 | 47 | 9 | 6 | 9 | 6 | 62 | NO | NO | NO | -20 | -23 | 13 | 220 | 10 | 11 | 3 | NO | NO | NO | 20 | 36 | 28 |
| 21 | 62 | 970951 | NO | NO | 0 | 36 | 26 | 34 | 45 | 9 | 6 | 9 | 6 | 64 | NO | NO | NO | -19 | -23 | 15 | 210 | 11 | 10 | 6 | NO | NO | NO | 0 | 35 | 27 |
| 22 | 33 | 927694 | NO | NO | 0 | 32 | 26 | 35 | 48 | 10 | 9 | 10 | 9 | 62 | NO | NO | NO | -19.2 | -24.8 | 13 | 210 | 11 | 11 | 2 | NO | NO | NO | 0 | 34 | 26 |
| 23 | 30 | 934307 | NO | NO | 0 | 36 | 25 | 35 | 49 | 9 | 7 | 9 | 6 | 64 | NO | NO | NO | -18.9 | -23 | 10 | 220 | 11 | 13 | 3 | NO | NO | NO | 0 | 35 | 25 |
| 24 | 53 | 930608 | NO | NO | 0 | 36 | 27 | 35 | 42 | 9 | 7 | 9 | 8 | 60 | NO | NO | NO | -18.8 | -25 | 12 | 198 | 11 | 15 | 4 | NO | NO | NO | 0 | 35 | 26 |
| 25 | 31 | 776090 | NO | NO | 0 | 35 | 22 | 35 | 46 | 10 | 9 | 9 | 6 | 62 | NO | NO | NO | -18 | -25.2 | 11 | 200 | 11 | 12 | 6 | NO | NO | NO | 0 | 35 | 24 |
| 26 | 65 | 971260 | NO | NO | 0 | 34 | 26 | 34 | 45 | 9 | 8 | 9 | 7 | 62 | NO | NO | NO | -19.2 | -22.5 | 12 | 210 | 11 | 13 | 6 | NO | NO | NO | 0 | 34 | 27 |
| 27 | 53 | 937614 | NO | NO | 0 | 34 | 26 | 33 | 46 | 9 | 8 | 9 | 8 | 62 | NO | NO | NO | -19.2 | -19.8 | 14 | 210 | 11 | 15 | 6 | NO | NO | NO | 0 | 31 | 25 |
| 28 | 52 | 970558 | NO | NO | 0 | 34 | 25 | 35 | 48 | 9 | 6 | 9 | 6 | 60 | NO | NO | NO | -19 | -20.4 | 12 | 210 | 11 | 13 | 5 | NO | NO | NO | 0 | 34 | 26 |
| 29 | 60 | 944390 | NO | NO | 0 | 32 | 26 | 35 | 46 | 9 | 7 | 9 | 6 | 58 | NO | NO | NO | -20 | -23 | 12 | 216 | 10 | 12 | 2 | NO | NO | NO | 0 | 34 | 25 |
| 30 | 50 | 772456 | NO | NO | 0 | 32 | 27 | 34 | 45 | 9 | 7 | 9 | 8 | 56 | NO | NO | NO | -19.8 | -22.4 | 13 | 210 | 11 | 13 | 4 | NO | NO | NO | 0 | 34 | 24 |
| 31 | 63 | 965930 | NO | NO | 0 | 34 | 25 | 35 | 47 | 9 | 8 | 9 | 7 | 56 | NO | NO | NO | -19 | -22.8 | 14 | 220 | 14 | 11 | 4 | NO | NO | NO | 0 | 34 | 26 |
| 32 | 53 | 866338 | NO | NO | 10 | 32 | 26 | 34 | 47 | 9 | 8 | 9 | 6 | 56 | NO | NO | NO | -20 | -24.3 | 13 | 210 | 10 | 13 | 4 | NO | NO | NO | 15 | 33 | 25 |
| 33 | 64 | 979946 | NO | NO | 0 | 32 | 26 | 34 | 47 | 10 | 9 | 9 | 6 | 62 | NO | NO | NO | -16 | -21 | 13 | 200 | 11 | 11 | 2 | NO | NO | NO | 0 | 33 | 24 |
| 34 | 59 | 976901 | NO | NO | 0 | 32 | 25 | 34 | 46 | 9 | 7 | 9 | 8 | 62 | NO | NO | NO | -15.6 | -20.2 | 13 | 210 | 11 | 12 | 4 | NO | NO | NO | 0 | 33 | 26 |
| 35 | 39 | 40436 | NO | NO | 0 | 30 | 20 | 34 | 46 | 9 | 6 | 9 | 7 | 64 | NO | NO | NO | -21 | -24 | 13 | 190 | 10 | 13 | 6 | NO | NO | NO | 0 | 32 | 21 |
| 36 | 33 | 982659 | NO | NO | 0 | 32 | 28 | 35 | 47 | 9 | 7 | 10 | 7 | 64 | NO | NO | NO | -18.7 | -21.4 | 13 | 207 | 11 | 12 | 6 | NO | NO | NO | 0 | 33 | 29 |
| 37 | 34 | 988212 | NO | NO | 0 | 32 | 25 | 37 | 49 | 9 | 8 | 9 | 7 | 62 | NO | NO | NO | 19.2 | -22.8 | 13 | 200 | 11 | 13 | 5 | NO | NO | NO | 0 | 33 | 24 |
| 38 | 51 | 994935 | NO | NO | 0 | 34 | 29 | 38 | 46 | 10 | 9 | 9 | 8 | 63 | NO | NO | NO | -20.2 | -24.8 | 15 | 210 | 10 | 13 | 4 | NO | NO | NO | 0 | 33 | 27 |
| 39 | 77 | 425488 | yes | NO | 28 | 44 | 22 | 30 | 46 | 13 | 12 | 13 | 11 | 62 | NO | NO | NO | -18.2 | 19.8 | 12 | 190 | 11 | 12 | 18 | NO | yes | NO | 30 | 44 | 20 |
| 40 | 45 | 1006735 | NO | NO | 0 | 32 | 26 | 34 | 48 | 9 | 6 | 9 | 6 | 62 | NO | NO | NO | -19 | -23.4 | 13 | 210 | 10 | 12 | 4 | NO | NO | NO | 0 | 33 | 24 |
| 41 | 38 | 997481 | NO | NO | 0 | 34 | 25 | 35 | 46 | 10 | 9 | 9 | 7 | 60 | NO | NO | NO | -19 | -23.8 | 12 | 220 | 10 | 10 | 4 | NO | NO | NO | 0 | 34 | 26 |
| 42 | 54 | 1019331 | NO | NO | 0 | 34 | 24 | 35 | 47 | 9 | 6 | 10 | 7 | 62 | NO | NO | NO | -19 | -23 | 13 | 200 | 10 | 11 | 3 | NO | NO | NO | 0 | 35 | 25 |
| 43 | 55 | 966571 | NO | NO | 0 | 34 | 26 | 34 | 47 | 9 | 6 | 9 | 6 | 62 | NO | NO | NO | -19.2 | -20.2 | 14 | 200 | 12 | 14 | 6 | NO | NO | NO | 0 | 34 | 26 |
| 44 | 55 | 806682 | NO | NO | 0 | 33 | 24 | 34 | 46 | 9 | 6 | 9 | 6 | 60 | NO | NO | NO | -19.8 | -24.2 | 13 | 190 | 11 | 13 | 2 | NO | NO | NO | 0 | 33 | 24 |
| 45 | 45 | 1012024 | NO | NO | 0 | 33 | 23 | 34 | 49 | 9 | 6 | 9 | 7 | 60 | NO | NO | NO | -20.2 | -24.5 | 13 | 200 | 9 | 12 | 4 | NO | NO | NO | 0 | 33 | 23 |
| 46 | 61 | 970851 | NO | NO | 0 | 32 | 23 | 34 | 48 | 9 | 6 | 9 | 6 | 62 | NO | NO | NO | -18 | -24.2 | 14 | 200 | 11 | 13 | 2 | NO | NO | NO | 0 | 33 | 24 |
| 47 | 55 | 564851 | NO | NO | 0 | 33 | 23 | 34 | 49 | 9 | 6 | 9 | 7 | 60 | NO | NO | NO | -20.2 | -24.5 | 13 | 200 | 9 | 12 | 4 | NO | NO | NO | 0 | 33 | 23 |
| 48 | 33 | 1048372 | NO | NO | 0 | 32 | 24 | 34 | 48 | 9 | 6 | 8 | 6 | 62 | NO | NO | NO | -18.9 | -23 | 12 | 196 | 11 | 14 | 5 | NO | NO | NO | 0 | 33 | 25 |
| 49 | 59 | 1031146 | NO | NO | 0 | 36 | 25 | 35 | 49 | 9 | 6 | 9 | 6 | 58 | NO | NO | NO | -19.2 | -22.4 | 13 | 198 | 12 | 13 | 4 | NO | NO | NO | 0 | 35 | 26 |
| 50 | 45 | 1070503 | NO | NO | 0 | 35 | 26 | 35 | 49 | 10 | 8 | 10 | 8 | 62 | NO | NO | NO | -18.4 | -22.2 | 13 | 190 | 11 | 12 | 4 | NO | NO | NO | 0 | 36 | 25 |
| 51 | 49 | 1064089 | NO | NO | 0 | 35 | 23 | 26 | 47 | 9 | 6 | 9 | 6 | 63 | NO | NO | NO | -18.9 | -22 | 13 | 206 | 12 | 9 | 3 | NO | NO | NO | 0 | 32 | 23 |
| 52 | 42 | 861342 | NO | NO | 0 | 34 | 23 | 35 | 48 | 10 | 7 | 9 | 6 | 64 | NO | NO | NO | -19.1 | -22.2 | 13 | 190 | 12 | 12 | 3 | NO | NO | NO | 0 | 34 | 24 |
| 53 | 48 | 806682 | NO | NO | 0 | 35 | 26 | 34 | 48 | 9 | 6 | 9 | 6 | 63 | NO | NO | NO | -18.2 | -23.3 | 13 | 190 | 11 | 13 | 3 | NO | NO | NO | 0 | 34 | 27 |
| 54 | 52 | 1083876 | NO | NO | 0 | 33 | 24 | 32 | 48 | 9 | 6 | 9 | 6 | 62 | NO | NO | NO | -19 | -22.8 | 12 | 190 | 11 | 13 | 2 | NO | NO | NO | 0 | 33 | 24 |
| 55 | 39 | 1098001 | NO | NO | 0 | 34 | 23 | 35 | 47 | 9 | 6 | 9 | 6 | 60 | NO | NO | NO | -18.9 | -25.2 | 12 | 210 | 10 | 13 | 3 | NO | NO | NO | 0 | 35 | 22 |
| 56 | 60 | 1010449 | NO | NO | 0 | 35 | 23 | 35 | 49 | 9 | 6 | 9 | 6 | 63 | NO | NO | NO | -17.9 | -23.2 | 13 | 230 | 13 | 10 | 5 | NO | NO | NO | 0 | 35 | 22 |
| 57 | 50 | 1048259 | NO | NO | 0 | 33 | 29 | 34 | 49 | 9 | 6 | 9 | 6 | 60 | NO | NO | NO | -18.2 | -22.4 | 13 | 190 | 10 | 13 | 3 | NO | NO | NO | 0 | 35 | 28 |
| 58 | 53 | 1016643 | NO | NO | 0 | 33 | 29 | 34 | 49 | 9 | 6 | 9 | 6 | 60 | NO | NO | NO | -18.2 | -22.4 | 13 | 190 | 10 | 13 | 3 | NO | NO | NO | 0 | 35 | 28 |

| Sr. No | Age | MRD No. | LVID (S) | LVID (D) | IVST (S) | IVST(D) | LVPW(S) | LVPW(D) | EF(%) | Mild LVD | Moderate LVD | Severe LVD | GLS(%) | GCS (%) | MAPSE | DT(ms) | e'(cm/s) | s'(cm/s) | E/e' | DD1 | DD2 | DD3 | PASP | LAVI | Aortic Root | LVID (S) | LVID (D) | IVST (S) | IVST(D) |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | 56 | 656237 | 34 | 46 | 9 | 6 | 9 | 7 | 57 | NO | NO | NO | -21 | -21 | 14 | 200 | 10 | 10 | 7 | NO | NO | NO | 0 | - | - | - | - | - | - |
| 2 | 63 | 869729 | 34 | 47 | 9 | 7 | 9 | 7 | 60 | NO | NO | NO | -20 | -20 | 12 | 210 | 10 | 12 | 6 | NO | NO | NO | 0 | - | - | - | - | - | - |
| 3 | 41 | 911336 | 34 | 47 | 9 | 7 | 9 | 7 | 62 | NO | NO | NO | -21 | -22 | 12 | 216 | 12 | 11 | 5 | NO | NO | NO | 10 | - | - | - | - | - | - |
| 4 | 61 | 669852 | 34 | 47 | 9 | 8 | 9 | 7 | 63 | NO | NO | NO | -19.7 | -19.8 | 12 | 218 | 11 | 11 | 8 | NO | NO | NO | 0 | - | - | - | - | - | - |
| 5 | 63 | 222118 | 34 | 47 | 9 | 8 | 9 | 7 | 62 | NO | NO | NO | -19.8 | -22.7 | 13 | 210 | 12 | 10 | 8 | NO | NO | NO | 0 | - | - | - | - | - | - |
| 6 | 34 | 943306 | 34 | 48 | 10 | 8 | 9 | 8 | 62 | NO | NO | NO | -20.9 | -19.7 | 12 | 182 | 10 | 12 | 3 | NO | NO | NO | 15 | - | - | - | - | - | - |
| 7 | 55 | 933316 | 34 | 45 | 11 | 10 | 11 | 11 | 64 | NO | NO | NO | -21.8 | -19.6 | 12 | 180 | 10 | 11 | 12 | yes | NO | NO | 15 | - | - | - | - | - | - |
| 8 | 50 | 933177 | 32 | 48 | 9 | 9 | 9 | 7 | 62 | NO | NO | NO | -19.4 | -22.4 | 11 | 198 | 10 | 12 | 4 | NO | NO | NO | 0 | - | - | - | - | - | - |
| 9 | 67 | 937187 | 30 | 45 | 10 | 9 | 10 | 9 | 63 | NO | NO | NO | 19.6 | -20 | 11 | 190 | 10 | 11 | 5 | NO | NO | NO | 0 | - | - | - | - | - | - |
| 10 | 55 | 934985 | 34 | 40 | 9 | 8 | 9 | 8 | 62 | NO | NO | NO | -19 | -20 | 11 | 190 | 11 | 11 | 11 | NO | NO | NO | 0 | - | - | - | - | - | - |
| 11 | 45 | 308735 | 34 | 46 | 9 | 8 | 9 | 8 | 60 | NO | NO | NO | -19 | -21 | 13 | 190 | 10 | 12 | 7 | NO | NO | NO | 0 | - | - | - | - | - | - |
| 12 | 56 | 955759 | 34 | 47 | 10 | 9 | 9 | 8 | 63 | NO | NO | NO | -20 | -20.5 | 13 | 206 | 11 | 12 | 5 | NO | NO | NO | 0 | - | - | - | - | - | - |
| 13 | 46 | 941607 | 33 | 42 | 9 | 7 | 9 | 6 | 60 | NO | NO | NO | -18.8 | -20 | 12 | 200 | 11 | 12 | 5 | NO | NO | NO | 0 | - | - | - | - | - | - |
| 14 | 35 | 953275 | 31 | 46 | 9 | 6 | 10 | 7 | 62 | NO | NO | NO | -19.8 | -22.2 | 13 | 205 | 10 | 10 | 6 | NO | NO | NO | 0 | - | - | - | - | - | - |
| 15 | 46 | 388958 | 32 | 48 | 9 | 7 | 9 | 7 | 60 | NO | NO | NO | -19.2 | -22.2 | 12 | 200 | 10 | 11 | 5 | NO | NO | NO | 0 | - | - | - | - | - | - |
| 16 | 42 | 405365 | 35 | 48 | 9 | 6 | 9 | 6 | 62 | NO | NO | NO | -18.9 | -23.4 | 12 | 210 | 11 | 11 | 4 | NO | NO | NO | 0 | - | - | - | - | - | - |
| 17 | 45 | 480775 | 35 | 48 | 9 | 6 | 9 | 6 | 62 | NO | NO | NO | -18.9 | -23.4 | 12 | 210 | 11 | 11 | 4 | NO | NO | NO | 0 | - | - | - | - | - | - |
| 18 | 53 | 859097 | 33 | 46 | 9 | 7 | 9 | 9 | 64 | NO | NO | NO | -19.9 | -23.4 | 12 | 220 | 10 | 11 | 3 | NO | NO | NO | 0 | - | - | - | - | - | - |
| 19 | 64 | 962661 | 35 | 47 | 9 | 6 | 9 | 7 | 62 | NO | NO | NO | -19.8 | -20.4 | 14 | 200 | 10 | 12 | 2 | NO | NO | NO | 16 | - | - | - | - | - | - |
| 20 | 55 | 955665 | 33 | 48 | 9 | 7 | 9 | 6 | 64 | NO | NO | NO | -19.8 | -22.9 | 12 | 210 | 10 | 11 | 4 | NO | NO | NO | 22 | - | - | - | - | - | - |
| 21 | 62 | 970951 | 34 | 48 | 9 | 6 | 9 | 6 | 64 | NO | NO | NO | -19 | -233 | 14 | 210 | 10 | 11 | 4 | NO | NO | NO | 0 | - | - | - | - | - | - |
| 22 | 33 | 927694 | 32 | 45 | 9 | 7 | 9 | 8 | 64 | NO | NO | NO | -19 | -23 | 12 | 210 | 11 | 12 | 4 | NO | NO | NO | 0 | - | - | - | - | - | - |
| 23 | 30 | 934307 | 35 | 48 | 9 | 8 | 9 | 6 | 68 | NO | NO | NO | -19 | 24.3 | 11 | 210 | 10 | 14 | 4 | NO | NO | NO | 0 | - | - | - | - | - | - |
| 24 | 53 | 930608 | 35 | 44 | 9 | 8 | 9 | 8 | 64 | NO | NO | NO | -18.4 | -25.8 | 13 | 200 | 11 | 14 | 3 | NO | NO | NO | 0 | - | - | - | - | - | - |
| 25 | 31 | 776090 | 34 | 48 | 9 | 7 | 9 | 6 | 64 | NO | NO | NO | -18.2 | -24.1 | 12 | 210 | 11 | 11 | 7 | NO | NO | NO | 0 | - | - | - | - | - | - |
| 26 | 65 | 971260 | 32 | 46 | 9 | 8 | 9 | 6 | 60 | NO | NO | NO | -19.9 | -23 | 12 | 220 | 10 | 13 | 4 | NO | NO | NO | 0 | - | - | - | - | - | - |
| 27 | 53 | 937614 | 34 | 48 | 9 | 6 | 9 | 8 | 64 | NO | NO | NO | -19 | -20.1 | 14 | 200 | 12 | 14 | 4 | NO | NO | NO | 0 | - | - | - | - | - | - |
| 28 | 52 | 970558 | 34 | 47 | 9 | 6 | 9 | 6 | 62 | NO | NO | NO | -19.2 | -20.2 | -19.2 | -20.2 | 12 | 14 | 4 | NO | NO | NO | 0 | - | - | - | - | - | - |
| 29 | 60 | 944390 | 34 | 46 | 9 | 7 | 9 | 6 | 58 | NO | NO | NO | -20.4 | -22.4 | 12 | 220 | 11 | 14 | 5 | NO | NO | NO | 0 | - | - | - | - | - | - |
| 30 | 50 | 772456 | 35 | 46 | 9 | 7 | 9 | 8 | 58 | NO | NO | NO | -19.5 | -19 | 12 | 200 | 12 | 14 | 3 | NO | NO | NO | 0 | - | - | - | - | - | - |
| 31 | 63 | 965930 | 34 | 48 | 9 | 7 | 9 | 6 | 57 | NO | NO | NO | 19.2 | -23.4 | 13 | 220 | 13 | 12 | 2 | NO | NO | NO | 0 | - | - | - | - | - | - |
| 32 | 53 | 866338 | 34 | 46 | 9 | 7 | 9 | 6 | 58 | NO | NO | NO | -19.6 | -23 | 12 | 205 | 11 | 12 | 4 | NO | NO | NO | 10 | - | - | - | - | - | - |
| 33 | 64 | 979946 | 35 | 45 | 10 | 9 | 9 | 8 | 64 | NO | NO | NO | -15.9 | -20.8 | 15 | 206 | 11 | 12 | 4 | NO | NO | NO | 0 | - | - | - | - | - | - |
| 34 | 59 | 976901 | 34 | 46 | 9 | 7 | 9 | 8 | 64 | NO | NO | NO | -16.1 | -21 | 12 | 210 | 10 | 12 | 6 | NO | NO | NO | 0 | - | - | - | - | - | - |
| 35 | 39 | 40436 | 35 | 45 | 10 | 6 | 9 | 6 | 63 | NO | NO | NO | -19.8 | -23.7 | 13 | 200 | 11 | 11 | 5 | NO | NO | NO | 0 | - | - | - | - | - | - |
| 36 | 33 | 982659 | 34 | 48 | 9 | 7 | 9 | 7 | 62 | NO | NO | NO | -18.9 | -21.8 | 12 | 208 | 10 | 11 | 4 | NO | NO | NO | 0 | - | - | - | - | - | - |
| 37 | 34 | 988212 | 34 | 48 | 9 | 7 | 9 | 7 | 60 | NO | NO | NO | -19 | -22.4 | 12 | 210 | 10 | 11 | 4 | NO | NO | NO | 0 | - | - | - | - | - | - |
| 38 | 51 | 994935 | 35 | 47 | 9 | 9 | 9 | 7 | 64 | NO | NO | NO | -20.1 | -24.9 | 14 | 230 | 10 | 12 | 4 | NO | NO | NO | 0 | - | - | - | - | - | - |
| 39 | 77 | 425488 | 32 | 46 | 13 | 11 | 13 | 12 | 60 | NO | NO | NO | -179 | -19.4 | 14 | 190 | 11 | 11 | 14 | NO | yes | NO | 30 | - | - | - | - | - | - |
| 40 | 45 | 1006735 | 35 | 49 | 9 | 7 | 9 | 6 | 60 | NO | NO | NO | -19.3 | -22.5 | 12 | 206 | 10 | 13 | 3 | NO | NO | NO | 0 | - | - | - | - | - | - |
| 41 | 38 | 997481 | 34 | 45 | 9 | 7 | 9 | 6 | 63 | NO | NO | NO | -18.4 | -22 | 12 | 230 | 11 | 11 | 3 | NO | NO | NO | 0 | - | - | - | - | - | - |
| 42 | 54 | 1019331 | 34 | 48 | 9 | 7 | 9 | 7 | 61 | NO | NO | NO | -18.9 | -23.3 | 13 | 190 | 10 | 12 | 2 | NO | NO | NO | 0 | - | - | - | - | - | - |
| 43 | 55 | 966571 | 34 | 47 | 9 | 6 | 9 | 6 | 62 | NO | NO | NO | -19.2 | -20.2 | 14 | 200 | 12 | 14 | 6 | NO | NO | NO | 0 | - | - | - | - | - | - |
| 44 | 55 | 806682 | 34 | 47 | 9 | 6 | 9 | 6 | 62 | NO | NO | NO | -19 | -24.8 | 13 | 190 | 10 | 12 | 4 | NO | NO | NO | 0 | - | - | - | - | - | - |
| 45 | 45 | 1012024 | 34 | 49 | 9 | 6 | 9 | 6 | 62 | NO | NO | NO | -18.9 | -22 | 12 | 190 | 10 | 12 | 3 | NO | NO | NO | 0 | - | - | - | - | - | - |
| 46 | 61 | 970851 | 35 | 47 | 9 | 6 | 9 | 6 | 62 | NO | NO | NO | -18.4 | -23.4 | 13 | 210 | 10 | 14 | 4 | NO | NO | NO | 0 | - | - | - | - | - | - |
| 47 | 55 | 564851 | 35 | 49 | 9 | 6 | 9 | 6 | 62 | NO | NO | NO | -18.9 | -22 | 12 | 190 | 10 | 12 | 3 | NO | NO | NO | 0 | - | - | - | - | - | - |
| 48 | 33 | 1048372 | 35 | 47 | 9 | 6 | 9 | 7 | 64 | NO | NO | NO | -18.7 | -22.6 | 13 | 210 | 10 | 12 | 4 | NO | NO | NO | 0 | - | - | - | - | - | - |
| 49 | 59 | 1031146 | 35 | 48 | 9 | 6 | 9 | 6 | 60 | NO | NO | NO | -18.8 | -22.5 | 14 | 190 | 11 | 12 | 3 | NO | NO | NO | 0 | - | - | - | - | - | - |
| 50 | 45 | 1070503 | 34 | 49 | 9 | 7 | 9 | 7 | 62 | NO | NO | NO | -19.2 | -21.4 | 12 | 189 | 10 | 12 | 3 | NO | NO | NO | 0 | - | - | - | - | - | - |
| 51 | 49 | 1064089 | 34 | 46 | 9 | 6 | 9 | 6 | 64 | NO | NO | NO | -19.7 | -21.9 | 12 | 210 | 12 | 10 | 5 | NO | NO | NO | 0 | - | - | - | - | - | - |
| 52 | 42 | 861342 | 35 | 48 | 9 | 6 | 9 | 7 | 62 | NO | NO | NO | -18.5 | -20.2 | 13 | 196 | 12 | 13 | 3 | NO | NO | NO | 0 | - | - | - | - | - | - |
| 53 | 48 | 806682 | 34 | 49 | 9 | 6 | 10 | 7 | 63 | NO | NO | NO | -18.6 | -23.4 | 13 | 200 | 12 | 12 | 4 | NO | NO | NO | 0 | - | - | - | - | - | - |
| 54 | 52 | 1083876 | 35 | 48 | 9 | 6 | 9 | 6 | 60 | NO | NO | NO | -19.2 | -24 | 12 | 190 | 11 | 12 | 4 | NO | NO | NO | 0 | - | - | - | - | - | - |
| 55 | 39 | 1098001 | 35 | 48 | 9 | 6 | 9 | 7 | 61 | NO | NO | NO | -21 | -25.4 | 13 | 220 | 11 | 12 | 4 | NO | NO | NO | 0 | - | - | - | - | - | - |
| 56 | 60 | 1010449 | 34 | 49 | 9 | 7 | 9 | 6 | 63 | NO | NO | NO | -18.2 | -22.2 | 12 | 220 | 12 | 12 | 3 | NO | NO | NO | 0 | - | - | - | - | - | - |
| 57 | 50 | 1048259 | 34 | 49 | 9 | 6 | 9 | 7 | 61 | NO | NO | NO | -18.4 | -23 | 13 | 188 | 11 | 12 | 5 | NO | NO | NO | 0 | - | - | - | - | - | - |
| 58 | 53 | 1016643 | 34 | 49 | 9 | 6 | 9 | 7 | 61 | NO | NO | NO | -18.4 | -23 | 13 | 188 | 11 | 12 | 5 | NO | NO | NO | 0 | - | - | - | - | - | - |

| Sr. No | Age | MRD No. | LVPW(S) | LVPW(D) | EF(%) | Mild LVD | Moderate LVD | Severe LVD | Full Recovery | Partial recovery | GLS(%) | GCS (%) | MAPSE | DT(ms) | e'(cm/s) | s'(cm/s) | E/e' | DD1 | DD2 | DD3 | PASP | RAS INHIBITORS | B Blockers | Diuretic | MRA |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | 56 | 656237 | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| 2 | 63 | 869729 | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| 3 | 41 | 911336 | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| 4 | 61 | 669852 | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| 5 | 63 | 222118 | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| 6 | 34 | 943306 | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| 7 | 55 | 933316 | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| 8 | 50 | 933177 | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| 9 | 67 | 937187 | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| 10 | 55 | 934985 | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| 11 | 45 | 308735 | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| 12 | 56 | 955759 | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| 13 | 46 | 941607 | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| 14 | 35 | 953275 | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| 15 | 46 | 388958 | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| 16 | 42 | 405365 | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| 17 | 45 | 480775 | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| 18 | 53 | 859097 | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| 19 | 64 | 962661 | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| 20 | 55 | 955665 | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| 21 | 62 | 970951 | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| 22 | 33 | 927694 | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| 23 | 30 | 934307 | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| 24 | 53 | 930608 | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| 25 | 31 | 776090 | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| 26 | 65 | 971260 | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| 27 | 53 | 937614 | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| 28 | 52 | 970558 | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| 29 | 60 | 944390 | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| 30 | 50 | 772456 | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| 31 | 63 | 965930 | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| 32 | 53 | 866338 | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| 33 | 64 | 979946 | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| 34 | 59 | 976901 | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| 35 | 39 | 40436 | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| 36 | 33 | 982659 | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| 37 | 34 | 988212 | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| 38 | 51 | 994935 | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| 39 | 77 | 425488 | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| 40 | 45 | 1006735 | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| 41 | 38 | 997481 | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| 42 | 54 | 1019331 | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| 43 | 55 | 966571 | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| 44 | 55 | 806682 | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| 45 | 45 | 1012024 | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| 46 | 61 | 970851 | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| 47 | 55 | 564851 | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| 48 | 33 | 1048372 | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| 49 | 59 | 1031146 | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| 50 | 45 | 1070503 | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| 51 | 49 | 1064089 | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| 52 | 42 | 861342 | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| 53 | 48 | 806682 | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| 54 | 52 | 1083876 | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| 55 | 39 | 1098001 | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| 56 | 60 | 1010449 | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| 57 | 50 | 1048259 | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| 58 | 53 | 1016643 | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - |

| Sr. No | Age | MRD No. | Hemoglobin | Albumin | HTN | SBP | DBP | DM | east involv | BMI | BSA | ER+ | PR+ | HER2+ | Cancer Stage | T | N | M | Surgery | RT dosage Gy | Doxorubicin | Cylophosphamide | Trastuzumab | Carboplatin |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 59 | 48 | 1048464 | 9.9 | 4.1 | No | 126 | 68 | No | Left | 35.92 | 1.71 | Negative | Negative | Positive | II | 3 | 2 | 0 | yes | 50 | - | - | 5450 | 3600 |
| 60 | 44 | 1111936 | 9.9 | 4.2 | No | 128 | 80 | No | Left | 27.48 | 1.59 | Negative | Negative | Negative | I | 2 | 0 | 0 | yes | No | 360 | 3600 | - | - |
| 61 | 43 | 1115341 | 9.8 | 3.9 | No | 126 | 70 | No | Left | 28.9 | 1.65 | Negative | Negative | Positive | III | 3 | 2 | 0 | yes | 42.5 | - | - | 3380 | 3600 |
| 62 | 49 | 1114221 | 11.7 | 4.2 | No | 118 | 60 | No | Right | 26.16 | 1.71 | Negative | Negative | Negative | I | 2 | 0 | 0 | yes | No | 400 | 4000 | - | - |
| 63 | 31 | 925015 | 7 | 3.2 | No | 110 | 68 | No | Right | 25.64 | 1.65 | Negative | Negative | Negative | II | 2 | 1 | 0 | yes | 42 | 200 | 2000 | - | 2050 |
| 64 | 55 | 1110120 | 10.3 | 3.8 | No | 112 | 60 | No | Left | 28 | 1.72 | negative | Negative | Positive | III | 4 | 2 | 0 | yes | 49.8 | - | - | 2780 | 3000 |
| 65 | 53 | 1060395 | 10.7 | 3.8 | No | 120 | 80 | No | Right | 23.92 | 1.68 | Negative | Positive | Positive | II | 2 | 0 | 0 | yes | No | - | - | 2660 | - |
| 66 | 50 | 1058831 | 10.2 | 4.1 | No | 126 | 82 | No | Right | 28 | 1.77 | Negative | Negative | Positive | II | 2 | 1 | 0 | yes | 50 | - | - | 3120 | 2600 |
| 67 | 50 | 1056921 | 9.8 | 5 | No | 134 | 82 | No | Left | 32.44 | 1.59 | Negative | Negative | Negative | I | 2 | 1 | 0 | yes | 52 | 360 | 3600 | - | - |
| 68 | 42 | 861342 | 10.1 | 4.3 | No | 122 | 78 | No | Right | 33.79 | 1.63 | Negative | Negative | Negative | I | 2 | 1 | 0 | yes | 50.4 | 360 | 3600 | - | - |
| 69 | 65 | 1155804 | 12 | 4.7 | No | 128 | 68 | No | Left | 24 | 1.87 | Positive | Positive | Positive | X | 3 | 2 | 0 | yes | 56 | 300 | 3000 | 3380 | 3600 |
| 70 | 38 | 1130260 | 11.4 | 4.1 | No | 133 | 78 | No | Left | 22.7 | 1.75 | Negative | Negative | Negative | III | 2 | 1 | 0 | yes | No | 400 | 4000 | - | - |
| 71 | 44 | 114709 | 7.6 | 3.9 | No | 120 | 70 | No | Left | 25 | 1.69 | Negative | Positive | Positive | II | 2 | 1 | 0 | yes | 37.18 | - | - | 1420 | 1800 |
| 72 | 66 | 657835 | 11.3 | 4.1 | No | 132 | 68 | No | Right | 24.52 | 1.56 | Negative | Negative | Positive | IV | 2 | 1 | 0 | yes | No | - | - | 4853 | - |
| 73 | 49 | 1102574 | 8.8 | 3.6 | No | 128 | 68 | No | Left | 23.37 | 1.66 | Negative | Positive | Positive | II | 2 | 0 | 0 | yes | 50 | - | - | 3730 | 3600 |
| 74 | 50 | 1187410 | 10 | 3.4 | No | 130 | 76 | No | Left | 25 | 1.74 | Negative | Negative | Negative | II | 3 | 2 | 1 | yes | No | 360 | 3600 | - | - |
| 75 | 53 | 1210637 | 10 | 3.8 | No | 127 | 67 | No | Right | 34.6 | 1.76 | Negative | Negative | Positive | III | 2 | 2 | 0 | yes | No | - | - | 680 | 600 |
| 76 | 44 | 1147409 | 9.9 | 3.7 | No | 128 | 78 | No | Right | 26 | 1.58 | Negative | Negative | Positive | II | 2 | 1 | 0 | yes | 37.17 | - | - | 2710 | 3150 |
| 77 | 54 | 1122653 | 11.3 | 3.6 | No | 120 | 60 | No | Right | 31.4 | 1.64 | Negative | Negative | Positive | II | 2 | 1 | 0 | yes | 50 | - | - | 3570 | 4800 |
| 78 | 44 | 719162 | 11 | 4.2 | No | 120 | 80 | No | Left | 26.4 | 1.65 | Negative | Positive | Positive | II | 2 | 0 | 0 | yes | No | - | - | 2660 | - |
| 79 | 74 | 968605 | 9.6 | 3.8 | No | 126 | 82 | No | Right | 24.7 | 1.68 | Negative | Negative | Positive | II | 2 | 1 | 0 | yes | No | - | - | 3120 | 2600 |
| 80 | 53 | 90718 | 7.5 | 4.8 | No | 120 | 80 | No | Right | 27.4 | 1.65 | Negative | Positive | Positive | II | 2 | 0 | 0 | yes | 50.4 | - | - | 2660 | - |
| 81 | 72 | 966863 | 11.8 | 3.4 | No | 126 | 82 | No | Left | 26.9 | 1.56 | Negative | Negative | Positive | II | 2 | 1 | 0 | yes | No | - | - | 3120 | 2600 |
| 82 | 72 | 926951 | 9.9 | 4 | No | 126 | 76 | no | Left | 26.3 | 1.62 | Positive | Positive | Negative | III | 3 | 3 | 0 | yes | No | 70 | 700 | - | - |
| 83 | 35 | 685078 | 11.9 | 3.9 | No | 122 | 78 | No | Left | 26 | 1.54 | Negative | Negative | Negative | I | 2 | 1 | 0 | yes | 50 | 360 | 3600 | - | - |
| 84 | 55 | 966571 | 10.9 | 3.9 | No | 122 | 70 | No | Right | 25.8 | 1.67 | negative | Negative | Negative | III | 2 | 3 | 0 | yes | No | 400 | 4000 | - | - |
| 85 | 52 | 932190 | 11.3 | 4.2 | yes | 128 | 80 | No | Left | 24.9 | 1.4 | negative | Negative | Positive | III | 3 | 2 | 0 | yes | 50.4 | 340 | 3480 | 1380 | - |
| 86 | 35 | 964110 | 9.6 | 3.8 | No | 130 | 76 | No | Left | 24.92 | 1.63 | Positive | Positive | Positive | III | 4 | 1 | 0 | yes | No | - | - | 1880 | 3000 |
| 87 | 48 | 980846 | 11.5 | 4.2 | No | 127 | 80 | No | Left | 18.87 | 1.54 | Negative | Negative | Negative | III | 2 | 1 | 0 | yes | No | 90 | 900 | - | 1200 |
| 88 | 61 | 699845 | 11.6 | 3.9 | No | 128 | 70 | No | Left | 42.22 | 1.8 | Negative | Negative | Negative | II | 2 | 0 | 0 | yes | No | - | 2910 | 896 | 875 |
| 89 | 54 | 972679 | 12 | 3.3 | No | 130 | 68 | No | Right | 40.89 | 1.8 | Negative | Negative | Negative | II | 1 | 1 | 0 | yes | 50.4 | 110 | 1100 | - | 2350 |
| 90 | 45 | 1030798 | 9.5 | 4.2 | No | 128 | 68 | No | Left | 28.6 | 1.36 | Positive | Positive | Positive | IV | 4 | 2 | 0 | yes | No | - | - | 1960 | - |
| 91 | 44 | 1017434 | 9.6 | 4.19 | No | 132 | 78 | No | Right | 34.65 | 1.64 | Negative | Negative | Negative | II | 1 | 1 | 0 | yes | No | 400 | 4000 | - | - |
| 92 | 46 | 427108 | 10.6 | 3.4 | No | 118 | 64 | No | Left | 29.6 | 1.6 | Negative | Positive | Positive | III | 4 | 2 | 0 | yes | 50 | 110 | 1100 | 1320 | - |
| 93 | 45 | 1012024 | 10.3 | 3.78 | YES | 132 | 78 | No | Bilateral | 24.69 | 1.78 | Negative | Negative | Positive | III | 3 | 2 | 0 | yes | 52 | 480 | 4900 | - | - |
| 94 | 53 | 1016643 | 12.9 | 4.5 | No | 118 | 70 | No | Left | 27.29 | 1.69 | Negative | Negative | Negative | III | 2 | 1 | 0 | yes | 50 | 380 | 3900 | - | - |
| 95 | 68 | 30415 | 11.5 | 4 | NO | 128 | 30 | no | Bilateral | 27.9 | 1.73 | Positive | Negative | Negative | IV | 2 | 3 | 1 | yes | 40 | - | - | - | 1350 |
| 96 | 51 | 663707 | 9.5 | 3.7 | No | 134 | 82 | No | Left | 33.59 | 1.68 | Negative | Negative | Positive | II | 2 | 1 | 0 | yes | 50 | 405 | 4050 | - | - |
| 97 | 55 | 966571 | 11.6 | 4 | No | 118 | 68 | No | Left | 28.28 | 1.71 | Negative | Negative | Negative | III | 3 | 3 | 0 | yes | No | 400 | 4000 | - | - |

| Sr. No | Age | MRD No. | Paclitaxel | Docetaxel | NYHA Class | BNP | Echo | LAVI | Aortic Root | LVID (S) | LVID (D) | IVST (S) | IVST(D) | LVPW(S) | LVPW(D) | EF(%) | Mild LVD | Moderate LVD | Severe LVD | GLS(%) | GCS (%) | MAPSE | DT(ms) | e'(cm/s) | s'(cm/s) | E/e' | DD1 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 59 | 48 | 1048464 | - | - | - | - | **1st** | 35 | 28 | 35 | 48 | 9 | 6 | 9 | 6 | 62 | NO | NO | NO | -18.2 | -24.8 | 12 | 200 | 12 | 12 | 2 | NO |
| 60 | 44 | 1111936 | - | - | - | - | **1st** | 35 | 28 | 35 | 48 | 9 | 6 | 9 | 6 | 62 | NO | NO | NO | -18.4 | -25.4 | 12 | 190 | 12 | 12 | 2 | NO |
| 61 | 43 | 1115341 | - | - | - | - | **1st** | 36 | 30 | 35 | 48 | 9 | 6 | 9 | 6 | 62 | NO | NO | NO | -19.8 | -22.8 | 12 | 190 | 11 | 12 | 2 | NO |
| 62 | 49 | 1114221 | - | - | - | - | **1st** | 35 | 28 | 35 | 48 | 9 | 7 | 9 | 6 | 62 | NO | NO | NO | -17.8 | -25 | 12 | 210 | 12 | 14 | 2 | NO |
| 63 | 31 | 925015 | 1200 | - | - | - | **1st** | 35 | 32 | 34 | 48 | 9 | 6 | 9 | 7 | 62 | NO | NO | NO | -18.2 | -24.2 | 14 | 220 | 12 | 12 | 2 | NO |
| 64 | 55 | 1110120 | - | - | - | - | **1st** | 36 | 35 | 34 | 48 | 9 | 6 | 9 | 6 | 62 | NO | NO | NO | -20.3 | -24.2 | 12 | 200 | 12 | 11 | 2 | NO |
| 65 | 53 | 1060395 | 2200 | - | - | - | **1st** | 34 | 29 | 35 | 49 | 9 | 6 | 9 | 6 | 54 | NO | NO | NO | -17.4 | -20.4 | 12 | 180 | 10 | 12 | 4 | NO |
| 66 | 50 | 1058831 | - | - | - | - | **1st** | 36 | 29 | 35 | 48 | 9 | 6 | 9 | 6 | 62 | NO | NO | NO | -19.4 | -20.4 | 12 | 210 | 11 | 12 | 3 | NO |
| 67 | 50 | 1056921 | 960 | - | - | - | **1st** | 34 | 29 | 35 | 48 | 9 | 6 | 9 | 6 | 58 | NO | NO | NO | -19.8 | -25.3 | 12 | 210 | 11 | 12 | 4 | NO |
| 68 | 42 | 861342 | 960 | - | - | - | **1st** | 35 | 29 | 35 | 48 | 9 | 6 | 9 | 6 | 62 | NO | NO | NO | -19.4 | -20.4 | 14 | 230 | 14 | 12 | 4 | NO |
| 69 | 65 | 1155804 | - | - | - | - | **1st** | 39 | 27 | 35 | 45 | 9 | 6 | 10 | 6 | 65 | NO | NO | NO | -19.5 | -21 | 12 | 180 | 12 | 12 | 4 | NO |
| 70 | 38 | 1130260 | - | - | - | - | **1st** | 35 | 27 | 34 | 45 | 10 | 6 | 9 | 7 | 58 | NO | NO | NO | -18.6 | -23 | 12 | 200 | 11 | 12 | 4 | NO |
| 71 | 44 | 114709 | - | - | - | - | **1st** | 34 | 26 | 36 | 46 | 10 | 6 | 9 | 6 | 63 | NO | NO | NO | -19.2 | -24 | 12 | 198 | 12 | 11 | 4 | NO |
| 72 | 66 | 657835 | - | - | - | - | **1st** | 34 | 28 | 35 | 46 | 10 | 7 | 9 | 6 | 62 | NO | NO | NO | -17.4 | -22.3 | 13 | 220 | 12 | 11 | 4 | NO |
| 73 | 49 | 1102574 | - | - | - | - | **1st** | 39 | 28 | 35 | 45 | 10 | 7 | 10 | 7 | 63 | NO | NO | NO | -17.2 | -23 | 12 | 220 | 11 | 11 | 4 | NO |
| 74 | 50 | 1187410 | - | - | - | - | **1st** | 34 | 28 | 35 | 46 | 10 | 7 | 9 | 6 | 62 | NO | NO | NO | -17.4 | -22.3 | 13 | 220 | 12 | 11 | 4 | NO |
| 75 | 53 | 1210637 | - | - | - | - | **1st** | 39 | 28 | 35 | 45 | 10 | 7 | 10 | 7 | 63 | NO | NO | NO | -17.2 | -23 | 12 | 220 | 11 | 11 | 4 | NO |
| 76 | 44 | 1147409 | - | - | - | - | **1st** | 34 | 28 | 35 | 46 | 10 | 7 | 9 | 6 | 62 | NO | NO | NO | -17.4 | -22.3 | 13 | 220 | 12 | 11 | 4 | NO |
| 77 | 54 | 1122653 | - | - | - | - | **1st** | 39 | 28 | 35 | 45 | 10 | 7 | 10 | 7 | 63 | NO | NO | NO | -17.2 | -23 | 12 | 220 | 11 | 11 | 4 | NO |
| 78 | 44 | 719162 | 2200 | - | - | - | **1st** | 34 | 26 | 36 | 46 | 10 | 6 | 9 | 6 | 63 | NO | NO | NO | -19.2 | -24 | 12 | 198 | 12 | 11 | 4 | NO |
| 79 | 74 | 968605 | - | - | - | - | **1st** | 34 | 28 | 35 | 46 | 10 | 7 | 9 | 6 | 62 | NO | NO | NO | -17.4 | -22.3 | 13 | 220 | 12 | 11 | 4 | NO |
| 80 | 53 | 90718 | 2200 | - | - | - | **1st** | 34 | 28 | 35 | 46 | 10 | 7 | 9 | 6 | 62 | NO | NO | NO | -17.4 | -22.3 | 13 | 220 | 12 | 11 | 4 | NO |
| 81 | 72 | 966863 | - | - | - | - | **1st** | 34 | 28 | 35 | 46 | 10 | 7 | 9 | 6 | 62 | NO | NO | NO | -17.4 | -22.3 | 13 | 220 | 12 | 11 | 4 | NO |
| 82 | 72 | 926951 | - | - | - | - | **1st** | 39 | 28 | 35 | 45 | 10 | 7 | 10 | 7 | 63 | NO | NO | NO | -17.2 | -23 | 12 | 220 | 11 | 11 | 4 | NO |
| 83 | 35 | 685078 | 960 | - | - | - | **1st** | 39 | 28 | 35 | 45 | 10 | 7 | 10 | 7 | 63 | NO | NO | NO | -17.2 | -23 | 12 | 220 | 11 | 11 | 4 | NO |
| 84 | 55 | 966571 | - | - | - | - | **1st** | 34 | 24 | 35 | 48 | 9 | 6 | 9 | 6 | 62 | NO | NO | NO | -19.4 | -24.3 | 12 | 200 | 10 | 12 | 4 | NO |
| 85 | 52 | 932190 | 720 | - | IV | Elevated | **1st** | 35 | 26 | 34 | 48 | 10 | 9 | 10 | 9 | 63 | NO | NO | NO | -19.8 | -26 | 12 | 200 | 12 | 12 | 4 | NO |
| 86 | 35 | 964110 | - | 600 | I | normal | **1st** | 36 | 28 | 34 | 47 | 9 | 9 | 9 | 7 | 60 | NO | NO | NO | -20 | -28 | 15 | 190 | 10 | 12 | 6 | NO |
| 87 | 48 | 980846 | 1860 | - | I | normal | **1st** | 36 | 26 | 33 | 45 | 10 | 7 | 9 | 6 | 62 | NO | NO | NO | -21 | -26 | 13 | 180 | 11 | 10 | 5 | NO |
| 88 | 61 | 699845 | - | 360 | I | normal | **1st** | 34 | 28 | 33 | 48 | 9 | 6 | 9 | 6 | 62 | NO | NO | NO | -18.3 | -22.8 | 12 | 190 | 10 | 12 | 4 | NO |
| 89 | 54 | 972679 | - | 480 | I |  | **1st** | 34 | 28 | 33 | 48 | 9 | 6 | 9 | 6 | 62 | NO | NO | NO | -18.3 | -22.8 | 12 | 190 | 10 | 12 | 4 | NO |
| 90 | 45 | 1030798 | - | 590 | I | normal | **1st** | 34 | 28 | 34 | 48 | 9 | 6 | 9 | 6 | 62 | NO | NO | NO | -18.3 | -22.8 | 12 | 190 | 10 | 12 | 4 | NO |
| 91 | 44 | 1017434 | 960 | - | I | normal | **1st** | 34 | 28 | 34 | 48 | 9 | 6 | 9 | 6 | 62 | NO | NO | NO | -18.3 | -22.8 | 12 | 190 | 10 | 12 | 4 | NO |
| 92 | 46 | 427108 | 1400 | - | I | normal | **1st** | 34 | 28 | 34 | 48 | 9 | 6 | 9 | 6 | 62 | NO | NO | NO | -18.3 | -22.8 | 12 | 190 | 10 | 12 | 4 | NO |
| 93 | 45 | 1012024 | - | - | I | normal | **1st** | 34 | 25 | 35 | 46 | 9 | 7 | 9 | 7 | 62 | NO | NO | NO | -18.9 | -24.2 | 14 | 198 | 10 | 12 | 4 | NO |
| 94 | 53 | 1016643 | - | - | I | normal | **1st** | 34 | 25 | 34 | 46 | 9 | 7 | 9 | 7 | 62 | NO | NO | NO | -22 | -24.2 | 14 | 198 | 10 | 12 | 4 | NO |
| 95 | 68 | 30415 | 2160 | - | I | normal | **1st** | 34 | 28 | 34 | 48 | 9 | 6 | 9 | 6 | 62 | NO | NO | NO | -18.3 | -22.8 | 12 | 190 | 10 | 12 | 4 | NO |
| 96 | 51 | 663707 | 1200 | - | I | normal | **1st** | 34 | 25 | 34 | 46 | 9 | 7 | 9 | 7 | 62 | NO | NO | NO | -18.9 | -24.2 | 14 | 198 | 10 | 12 | 4 | NO |
| 97 | 55 | 966571 | - | - | I | normal | **1st** | 34 | 25 | 34 | 46 | 9 | 7 | 9 | 7 | 62 | NO | NO | NO | -18.9 | -24.2 | 14 | 198 | 10 | 12 | 4 | NO |

| Sr. No | Age | MRD No. | DD2 | DD3 | PASP | LAVI | Aortic Root | LVID (S) | LVID (D) | IVST (S) | IVST(D) | LVPW(S) | LVPW(D) | EF(%) | mild LVD | Moderate LVD | Severe LVD | GLS(%) | GCS (%) | MAPSE | DT(ms) | e'(cm/s) | s'(cm/s) | E/e' | DD1 | DD2 | DD3 | PASP | LAVI | Aortic Root |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 59 | 48 | 1048464 | NO | NO | 0 | 36 | 26 | 34 | 49 | 9 | 7 | 10 | 7 | 63 | NO | NO | NO | -19.2 | -24.8 | 14 | 190 | 10 | 13 | 4 | NO | NO | NO | 0 | 35 | 29 |
| 60 | 44 | 1111936 | NO | NO | 0 | 36 | 30 | 34 | 49 | 9 | 7 | 9 | 6 | 61 | NO | NO | NO | -17.9 | -23.4 | 13 | 200 | 13 | 13 | 3 | NO | NO | NO | 0 | 37 | 31 |
| 61 | 43 | 1115341 | NO | NO | 0 | 36 | 31 | 34 | 49 | 9 | 6 | 9 | 7 | 63 | NO | NO | NO | -20.2 | -23.4 | 15 | 190 | 12 | 15 | 4 | NO | NO | NO | 0 | 35 | 32 |
| 62 | 49 | 1114221 | NO | NO | 0 | 36 | 26 | 34 | 48 | 9 | 6 | 9 | 7 | 63 | NO | NO | NO | -18.2 | -23.8 | 14 | 216 | 12 | 14 | 3 | NO | NO | NO | 0 | 36 | 25 |
| 63 | 31 | 925015 | NO | NO | 0 | 34 | 34 | 34 | 48 | 9 | 7 | 9 | 6 | 61 | NO | NO | NO | -20.4 | -24.8 | 15 | 216 | 12 | 13 | 3 | NO | NO | NO | 0 | 39 | 35 |
| 64 | 55 | 1110120 | NO | NO | 0 | 39 | 36 | 34 | 49 | 9 | 6 | 9 | 7 | 58 | NO | NO | NO | -19.2 | -21.4 | 15 | 190 | 15 | 12 | 4 | NO | NO | NO | 0 | 40 | 35 |
| 65 | 53 | 1060395 | NO | NO | 0 | 35 | 32 | 36 | 48 | 9 | 7 | 9 | 7 | 55 | NO | NO | NO | -18.1 | -23.2 | 15 | 170 | 11 | 15 | 3 | NO | NO | NO | 0 | 36 | 34 |
| 66 | 50 | 1058831 | NO | NO | 0 | 35 | 31 | 35 | 49 | 9 | 7 | 9 | 6 | 64 | NO | NO | NO | -18.4 | -21.3 | 15 | 212 | 11 | 13 | 4 | NO | NO | NO | 0 | 34 | 34 |
| 67 | 50 | 1056921 | NO | NO | 0 | 39 | 30 | 35 | 49 | 9 | 7 | 9 | 7 | 64 | NO | NO | NO | -19.4 | -24.9 | 15 | 200 | 11 | 15 | 3 | NO | NO | NO | 0 | 39 | 32 |
| 68 | 42 | 861342 | NO | NO | 0 | 39 | 28 | 35 | 47 | 9 | 7 | 9 | 7 | 60 | NO | NO | NO | -21 | -23.4 | 15 | 230 | 15 | 12 | 5 | NO | NO | NO | 0 | 35 | 29 |
| 69 | 65 | 1155804 | NO | NO | 0 | 35 | 28 | 35 | 46 | 10 | 7 | 9 | 7 | 64 | NO | NO | NO | -18.4 | -22.3 | 14 | 190 | 11 | 12 | 5 | NO | NO | NO | 0 | 38 | 29 |
| 70 | 38 | 1130260 | NO | NO | 0 | 33 | 28 | 35 | 46 | 9 | 7 | 9 | 7 | 58 | NO | NO | NO | -17.6 | -23.6 | 14 | 207 | 12 | 13 | 3 | NO | NO | NO | 0 | 35 | 30 |
| 71 | 44 | 114709 | NO | NO | 0 | 33 | 28 | 35 | 46 | 9 | 7 | 9 | 7 | 66 | NO | NO | NO | -17.8 | -22 | 13 | 210 | 12 | 12 | 5 | NO | NO | NO | 0 | 34 | 27 |
| 72 | 66 | 657835 | NO | NO | 0 | 34 | 28 | 33 | 46 | 10 | 7 | 9 | 7 | 64 | NO | NO | NO | -16.8 | -23.7 | 12 | 210 | 11 | 11 | 3 | NO | NO | NO | 0 | 35 | 29 |
| 73 | 49 | 1102574 | NO | NO | 0 | 35 | 29 | 33 | 47 | 9 | 6 | 9 | 7 | 64 | NO | NO | NO | -16.8 | -26 | 13 | 210 | 11 | 12 | 5 | NO | NO | NO | 0 | 35 | 29 |
| 74 | 50 | 1187410 | NO | NO | 0 | 34 | 28 | 33 | 46 | 10 | 7 | 9 | 7 | 64 | NO | NO | NO | -16.8 | -23.7 | 12 | 210 | 11 | 11 | 3 | NO | NO | NO | 0 | 35 | 29 |
| 75 | 53 | 1210637 | NO | NO | 0 | 35 | 29 | 33 | 47 | 9 | 6 | 9 | 7 | 64 | NO | NO | NO | -16.8 | -26 | 13 | 210 | 11 | 12 | 5 | NO | NO | NO | 0 | 35 | 29 |
| 76 | 44 | 1147409 | NO | NO | 0 | 34 | 28 | 33 | 46 | 10 | 7 | 9 | 7 | 64 | NO | NO | NO | -16.8 | -23.7 | 12 | 210 | 11 | 11 | 3 | NO | NO | NO | 0 | 35 | 29 |
| 77 | 54 | 1122653 | NO | NO | 0 | 35 | 29 | 34 | 47 | 9 | 6 | 9 | 7 | 64 | NO | NO | NO | -16.8 | -26 | 13 | 210 | 11 | 12 | 5 | NO | NO | NO | 0 | 35 | 29 |
| 78 | 44 | 719162 | NO | NO | 0 | 33 | 28 | 35 | 46 | 9 | 7 | 9 | 7 | 66 | NO | NO | NO | -17.8 | -22 | 13 | 210 | 12 | 12 | 5 | NO | NO | NO | 0 | 34 | 27 |
| 79 | 74 | 968605 | NO | NO | 0 | 34 | 28 | 35 | 46 | 10 | 7 | 9 | 7 | 64 | NO | NO | NO | -16.8 | -23.7 | 12 | 210 | 11 | 11 | 3 | NO | NO | NO | 0 | 35 | 29 |
| 80 | 53 | 90718 | NO | NO | 0 | 34 | 28 | 34 | 46 | 10 | 7 | 9 | 7 | 64 | NO | NO | NO | -16.8 | -23.7 | 12 | 210 | 11 | 11 | 3 | NO | NO | NO | 0 | 35 | 29 |
| 81 | 72 | 966863 | NO | NO | 0 | 34 | 28 | 34 | 46 | 10 | 7 | 9 | 7 | 64 | NO | NO | NO | -16.8 | -23.7 | 12 | 210 | 11 | 11 | 3 | NO | NO | NO | 0 | 35 | 29 |
| 82 | 72 | 926951 | NO | NO | 0 | 35 | 29 | 34 | 47 | 9 | 6 | 9 | 7 | 64 | NO | NO | NO | -16.8 | -26 | 13 | 210 | 11 | 12 | 5 | NO | NO | NO | 0 | 35 | 29 |
| 83 | 35 | 685078 | NO | NO | 0 | 35 | 29 | 34 | 47 | 9 | 6 | 9 | 7 | 64 | NO | NO | NO | -16.8 | -26 | 13 | 210 | 11 | 12 | 5 | NO | NO | NO | 0 | 35 | 29 |
| 84 | 55 | 966571 | NO | NO | 0 | 33 | 23 | 34 | 49 | 9 | 6 | 9 | 7 | 60 | NO | NO | NO | -20.2 | -24.5 | 13 | 200 | 9 | 12 | 4 | NO | NO | NO | 0 | 33 | 23 |
| 85 | 52 | 932190 | NO | NO | 0 | 34 | 28 | 34 | 49 | 10 | 9 | 10 | 9 | 53 | NO | NO | NO | -18.9 | -20.2 | 12 | 260 | 10 | 12 | 8 | NO | NO | NO | 0 | 38 | 27 |
| 86 | 35 | 964110 | NO | NO | 0 | 34 | 27 | 35 | 53 | 9 | 6 | 9 | 6 | 30 | NO | NO | YES | -12 | -18 | 8 | 230 | 6 | 7 | 13 | NO | NO | NO | 20 | 35 | 28 |
| 87 | 48 | 980846 | NO | NO | 0 | 34 | 28 | 36 | 48 | 9 | 6 | 9 | 6 | 38 | NO | YES | NO | -11 | -19 | 9 | 250 | 8 | 8 | 16 | YES | NO | NO | 28 | 36 | 28 |
| 88 | 61 | 699845 | NO | NO | 0 | 33 | 24 | 35 | 49 | 9 | 6 | 9 | 6 | 60 | NO | NO | NO | -16.7 | -20.4 | 12 | 220 | 11 | 10 | 8 | NO | NO | NO | 0 | 33 | 26 |
| 89 | 54 | 972679 | NO | NO | 0 | 33 | 24 | 34 | 50 | 9 | 6 | 9 | 6 | 46 | YES | NO | NO | -14 | -20.4 | 10 | 220 | 8 | 9 | 12 | NO | NO | NO | 0 | 33 | 26 |
| 90 | 45 | 1030798 | NO | NO | 0 | 33 | 24 | 33 | 50 | 9 | 6 | 9 | 6 | 36 | NO | YES | NO | -12 | -19 | 8 | 260 | 7 | 8 | 12 | YES | NO | NO | 0 | 33 | 26 |
| 91 | 44 | 1017434 | NO | NO | 0 | 33 | 24 | 33 | 48 | 9 | 6 | 9 | 6 | 53 | NO | NO | NO | -18.2 | -21 | 10 | 220 | 8 | 12 | 12 | NO | NO | NO | 0 | 33 | 26 |
| 92 | 46 | 427108 | NO | NO | 0 | 32 | 26 | 34 | 50 | 9 | 6 | 9 | 6 | 38 | NO | YES | NO | -13 | -18 | 8 | 210 | 7 | 8 | 12 | NO | NO | NO | 0 | 33 | 26 |
| 93 | 45 | 1012024 | NO | NO | 0 | 34 | 24 | 35 | 47 | 9 | 7 | 9 | 7 | 64 | NO | NO | NO | -19.2 | -25 | 12 | 210 | 11 | 13 | 12 | NO | NO | NO | 0 | 36 | 26 |
| 94 | 53 | 1016643 | NO | NO | 0 | 33 | 24 | 34 | 47 | 9 | 7 | 9 | 7 | 64 | NO | NO | NO | -21 | -25 | 13 | 210 | 11 | 13 | 12 | NO | NO | NO | 0 | 36 | 26 |
| 95 | 68 | 30415 | NO | NO | 0 | 33 | 24 | 34 | 50 | 9 | 6 | 9 | 6 | 32 | NO | YES | NO | -12.3 | -16.5 | 8 | 220 | 8 | 8 | 14 | NO | NO | NO | 0 | 33 | 26 |
| 96 | 51 | 663707 | NO | NO | 0 | 34 | 24 | 33 | 47 | 9 | 7 | 9 | 7 | 64 | NO | NO | NO | -19.2 | -25 | 13 | 210 | 11 | 13 | 12 | NO | NO | NO | 0 | 36 | 26 |
| 97 | 55 | 966571 | NO | NO | 0 | 35 | 24 | 33 | 47 | 9 | 7 | 9 | 7 | 60 | NO | NO | NO | -18.3 | -20 | 12 | 210 | 6 | 11 | 12 | NO | NO | NO | 0 | 36 | 26 |

| Sr. No | Age | MRD No. | LVID (S) | LVID (D) | IVST (S) | IVST(D) | LVPW(S) | LVPW(D) | EF(%) | Mild LVD | Moderate LVD | Severe LVD | GLS(%) | GCS (%) | MAPSE | DT(ms) | e'(cm/s) | s'(cm/s) | E/e' | DD1 | DD2 | DD3 | PASP | LAVI | Aortic Root | LVID (S) | LVID (D) | IVST (S) | IVST(D) |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 59 | 48 | 1048464 | 34 | 48 | 9 | 6 | 9 | 7 | 64 | NO | NO | NO | -19.1 | -24 | 15 | 186 | 12 | 12 | 3 | NO | NO | NO | 0 | - | - | - | - | - | - |
| 60 | 44 | 1111936 | 34 | 47 | 9 | 6 | 9 | 6 | 60 | NO | NO | NO | -19.2 | -22 | 14 | 210 | 12 | 12 | 5 | NO | NO | NO | 0 | - | - | - | - | - | - |
| 61 | 43 | 1115341 | 34 | 46 | 9 | 7 | 9 | 6 | 63 | NO | NO | NO | -20.3 | -24 | 14 | 200 | 11 | 13 | 3 | NO | NO | NO | 0 | - | - | - | - | - | - |
| 62 | 49 | 1114221 | 34 | 47 | 9 | 6 | 9 | 6 | 62 | NO | NO | NO | -19.2 | -22.9 | 15 | 220 | 12 | 13 | 2 | NO | NO | NO | 0 | - | - | - | - | - | - |
| 63 | 31 | 925015 | 34 | 48 | 9 | 7 | 9 | 7 | 60 | NO | NO | NO | -20.2 | -23.2 | 14 | 220 | 12 | 13 | 3 | NO | NO | NO | 0 | - | - | - | - | - | - |
| 64 | 55 | 1110120 | 33 | 48 | 9 | 7 | 9 | 7 | 55 | NO | NO | NO | -18.4 | -20.9 | 12 | 188 | 12 | 12 | 5 | NO | NO | NO | 0 | - | - | - | - | - | - |
| 65 | 53 | 1060395 | 34 | 48 | 9 | 7 | 9 | 7 | 55 | NO | NO | NO | -17.1 | -23.4 | 12 | 198 | 11 | 13 | 3 | NO | NO | NO | 0 | - | - | - | - | - | - |
| 66 | 50 | 1058831 | 34 | 49 | 9 | 7 | 9 | 7 | 63 | NO | NO | NO | -18.2 | -19.9 | 13 | 220 | 11 | 12 | 4 | NO | NO | NO | 0 | - | - | - | - | - | - |
| 67 | 50 | 1056921 | 34 | 47 | 9 | 7 | 9 | 7 | 63 | NO | NO | NO | -18.3 | -22.4 | 14 | 200 | 11 | 14 | 4 | NO | NO | NO | 0 | - | - | - | - | - | - |
| 68 | 42 | 861342 | 34 | 46 | 9 | 7 | 9 | 7 | 64 | NO | NO | NO | -18 | -22.7 | 14 | 220 | 14 | 13 | 4 | NO | NO | NO | 0 | - | - | - | - | - | - |
| 69 | 65 | 1155804 | 35 | 45 | 9 | 7 | 9 | 7 | 64 | NO | NO | NO | -18.2 | -23.1 | 13 | 197 | 11 | 12 | 3 | NO | NO | NO | 0 | - | - | - | - | - | - |
| 70 | 38 | 1130260 | 35 | 47 | 9 | 7 | 9 | 6 | 60 | NO | NO | NO | -17.6 | -25 | 13 | 210 | 12 | 11 | 4 | NO | NO | NO | 0 | - | - | - | - | - | - |
| 71 | 44 | 114709 | 34 | 45 | 9 | 7 | 9 | 7 | 65 | NO | NO | NO | -17.2 | -24.3 | 12 | 220 | 12 | 11 | 3 | NO | NO | NO | 0 | - | - | - | - | - | - |
| 72 | 66 | 657835 | 35 | 45 | 9 | 6 | 9 | 7 | 65 | NO | NO | NO | -17.8 | -21.3 | 12 | 208 | 12 | 11 | 5 | NO | NO | NO | 0 | - | - | - | - | - | - |
| 73 | 49 | 1102574 | 34 | 47 | 9 | 6 | 9 | 7 | 65 | NO | NO | NO | -17.8 | -24.6 | 12 | 208 | 13 | 12 | 4 | NO | NO | NO | 0 | - | - | - | - | - | - |
| 74 | 50 | 1187410 | 35 | 45 | 9 | 6 | 9 | 7 | 65 | NO | NO | NO | -17.8 | -21.3 | 12 | 208 | 12 | 11 | 5 | NO | NO | NO | 0 | - | - | - | - | - | - |
| 75 | 53 | 1210637 | 36 | 47 | 9 | 6 | 9 | 7 | 65 | NO | NO | NO | -17.8 | -24.6 | 12 | 208 | 13 | 12 | 4 | NO | NO | NO | 0 | - | - | - | - | - | - |
| 76 | 44 | 1147409 | 35 | 45 | 9 | 6 | 9 | 7 | 65 | NO | NO | NO | -17.8 | -21.3 | 12 | 208 | 12 | 11 | 5 | NO | NO | NO | 0 | - | - | - | - | - | - |
| 77 | 54 | 1122653 | 36 | 47 | 9 | 6 | 9 | 7 | 65 | NO | NO | NO | -17.8 | -24.6 | 12 | 208 | 13 | 12 | 4 | NO | NO | NO | 0 | - | - | - | - | - | - |
| 78 | 44 | 719162 | 36 | 45 | 9 | 7 | 9 | 7 | 65 | NO | NO | NO | -17.2 | -24.3 | 12 | 220 | 12 | 11 | 3 | NO | NO | NO | 0 | - | - | - | - | - | - |
| 79 | 74 | 968605 | 35 | 45 | 9 | 6 | 9 | 7 | 65 | NO | NO | NO | -17.8 | -21.3 | 12 | 208 | 12 | 11 | 5 | NO | NO | NO | 0 | - | - | - | - | - | - |
| 80 | 53 | 90718 | 35 | 45 | 9 | 6 | 9 | 7 | 65 | NO | NO | NO | -17.8 | -21.3 | 12 | 208 | 12 | 11 | 5 | NO | NO | NO | 0 | - | - | - | - | - | - |
| 81 | 72 | 966863 | 35 | 45 | 9 | 6 | 9 | 7 | 65 | NO | NO | NO | -17.8 | -21.3 | 12 | 208 | 12 | 11 | 5 | NO | NO | NO | 0 | - | - | - | - | - | - |
| 82 | 72 | 926951 | 36 | 47 | 9 | 6 | 9 | 7 | 65 | NO | NO | NO | -17.8 | -24.6 | 12 | 208 | 13 | 12 | 4 | NO | NO | NO | 0 | - | - | - | - | - | - |
| 83 | 35 | 685078 | 34 | 47 | 9 | 6 | 9 | 7 | 65 | NO | NO | NO | -17.8 | -24.6 | 12 | 208 | 13 | 12 | 4 | NO | NO | NO | 0 | - | - | - | - | - | - |
| 84 | 55 | 966571 | 34 | 49 | 9 | 6 | 9 | 6 | 62 | NO | NO | NO | -18.9 | -22 | 12 | 190 | 10 | 12 | 3 | NO | NO | NO | 0 | - | - | - | - | - | - |
| 85 | 52 | 932190 | 33 | 50 | 10 | 9 | 10 | 9 | 46 | YES | NO | NO | -15 | -19.1 | 9 | 250 | 9 | 9 | 14 | YES | NO | NO | 26 | 38 | 26 | 34 | 49 | 10 | 9 |
| 86 | 35 | 964110 | 35 | 50 | 9 | 6 | 9 | 6 | 42 | YES | NO | NO | -13 | -19 | 9 | 220 | 8 | 9 | 8 | NO | NO | NO | 15 | 36 | 28 | 34 | 48 | 9 | 6 |
| 87 | 48 | 980846 | 35 | 49 | 9 | 6 | 9 | 6 | 40 | NO | YES | NO | -14 | -21 | 8 | 220 | 7 | 9 | 12 | NO | NO | NO | 10 | 36 | 27 | 36 | 49 | 9 | 6 |
| 88 | 61 | 699845 | 35 | 48 | 9 | 6 | 9 | 6 | 46 | YES | NO | NO | -12 | -18 | 9 | 230 | 7 | 8 | 12 | NO | NO | NO | 0 | 32 | 26 | 34 | 49 | 9 | 6 |
| 89 | 54 | 972679 | 34 | 48 | 9 | 6 | 9 | 6 | 48 | YES | NO | NO | -14 | -21 | 9 | 230 | 9 | 9 | 8 | NO | NO | NO | 0 | 32 | 26 | 34 | 49 | 9 | 6 |
| 90 | 45 | 1030798 | 33 | 48 | 9 | 6 | 9 | 6 | 42 | YES | NO | NO | -14 | -21 | 9 | 250 | 9 | 9 | 8 | YES | NO | NO | 0 | 32 | 26 | 34 | 49 | 9 | 6 |
| 91 | 44 | 1017434 | 33 | 50 | 9 | 6 | 9 | 6 | 45 | YES | NO | NO | -16.2 | -19.1 | 9 | 230 | 9 | 9 | 8 | NO | NO | NO | 0 | 32 | 26 | 34 | 49 | 9 | 6 |
| 92 | 46 | 427108 | 34 | 48 | 9 | 6 | 9 | 6 | 42 | YES | NO | NO | -14 | -21 | 10 | 230 | 9 | 9 | 8 | NO | NO | NO | 0 | 32 | 26 | 34 | 49 | 9 | 6 |
| 93 | 45 | 1012024 | 34 | 46 | 9 | 6 | 9 | 7 | 50 | YES | NO | NO | -18 | -20 | 11 | 220 | 10 | 10 | 10 | NO | NO | NO | 0 | 34 | 25 | 37 | 52 | 9 | 8 |
| 94 | 53 | 1016643 | 34 | 46 | 9 | 6 | 9 | 7 | 48 | YES | NO | NO | -14.8 | -19.8 | 10 | 220 | 8 | 9.4 | 10 | NO | NO | NO | 0 | 34 | 25 | 34 | 48 | 9 | 8 |
| 95 | 68 | 30415 | 36 | 52 | 9 | 6 | 9 | 6 | 36 | NO | YES | NO | -13 | -16.9 | 9 | 246 | 9 | 7 | 14 | YES | NO | NO | 30 | 32 | 26 | 35 | 50 | 9 | 6 |
| 96 | 51 | 663707 | 34 | 49 | 9 | 6 | 9 | 7 | 40 | YES | NO | NO | -15 | -21 | 10 | 220 | 10 | 9 | 10 | NO | NO | NO | 0 | 34 | 25 | 34 | 48 | 9 | 8 |
| 97 | 55 | 966571 | 34 | 49 | 9 | 6 | 9 | 7 | 40 | YES | NO | NO | -15 | -22 | 9 | 220 | 10 | 9 | 9 | NO | NO | NO | 0 | 34 | 25 | 34 | 48 | 9 | 8 |

| Sr. No | Age | MRD No. | LVPW(S) | LVPW(D) | EF(%) | Mild LVD | Moderate LVD | Severe LVD | Full Recovery | Partial recovery | GLS(%) | GCS (%) | MAPSE | DT(ms) | e'(cm/s) | s'(cm/s) | E/e' | DD1 | DD2 | DD3 | PASP | RAS INHIBITORS | B Blockers | Diuretic | MRA |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 59 | 48 | 1048464 | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| 60 | 44 | 1111936 | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| 61 | 43 | 1115341 | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| 62 | 49 | 1114221 | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| 63 | 31 | 925015 | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| 64 | 55 | 1110120 | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| 65 | 53 | 1060395 | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| 66 | 50 | 1058831 | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| 67 | 50 | 1056921 | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| 68 | 42 | 861342 | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| 69 | 65 | 1155804 | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| 70 | 38 | 1130260 | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| 71 | 44 | 114709 | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| 72 | 66 | 657835 | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| 73 | 49 | 1102574 | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| 74 | 50 | 1187410 | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| 75 | 53 | 1210637 | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| 76 | 44 | 1147409 | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| 77 | 54 | 1122653 | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| 78 | 44 | 719162 | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| 79 | 74 | 968605 | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| 80 | 53 | 90718 | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| 81 | 72 | 966863 | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| 82 | 72 | 926951 | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| 83 | 35 | 685078 | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| 84 | 55 | 966571 | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| 85 | 52 | 932190 | 10 | 9 | 53 | NO | NO | NO | YES | - | NO | -15 | -22.8 | 10 | 220 | 12 | 12 | 8 | 0 | 0 | 0 | YES | YES | YES | YES |
| 86 | 35 | 964110 | 9 | 6 | 55 | NO | NO | NO | YES | - | NO | -18 | -22.7 | 12 | 196 | 10 | 11 | 6 | 0 | 0 | 0 | YES | YES | NO | NO |
| 87 | 48 | 980846 | 9 | 6 | 48 | YES | NO | NO | NO | YES | NO | -15 | -22.6 | 9 | 220 | 9 | 9 | 12 | 0 | 0 | 0 | YES | YES | NO | NO |
| 88 | 61 | 699845 | 9 | 7 | 55 | NO | NO | NO | YES | - | NO | -19.4 | -22.2 | 12 | 210 | 10 | 12 | 8 | 0 | 0 | 0 | YES | YES | NO | NO |
| 89 | 54 | 972679 | 9 | 7 | 56 | NO | NO | NO | YES | - | NO | -18.4 | -22.3 | 12 | 210 | 10 | 12 | 8 | 0 | 0 | 0 | YES | YES | NO | NO |
| 90 | 45 | 1030798 | 9 | 7 | 54 | NO | NO | NO | YES | - | NO | -18.6 | -21.9 | 12 | 210 | 10 | 12 | 8 | 0 | 0 | 0 | YES | YES | NO | NO |
| 91 | 44 | 1017434 | 9 | 7 | 54 | NO | NO | NO | YES | - | NO | -18.4 | -22.1 | 12 | 210 | 10 | 12 | 8 | 0 | 0 | 0 | YES | YES | NO | NO |
| 92 | 46 | 427108 | 9 | 7 | 60 | NO | NO | NO | YES | - | NO | -19.2 | -21.5 | 12 | 210 | 10 | 12 | 8 | 0 | 0 | 0 | YES | YES | NO | NO |
| 93 | 45 | 1012024 | 9 | 6 | 46 | YES | NO | NO | NO | YES | YES | -16 | -19.4 | 10 | 200 | 10 | 12 | 6 | 0 | 0 | 0 | YES | YES | NO | NO |
| 94 | 53 | 1016643 | 9 | 6 | 64 | NO | NO | NO | YES | - | NO | -21.4 | -27.2 | 12 | 200 | 10 | 12 | 6 | 0 | 0 | 0 | YES | YES | NO | NO |
| 95 | 68 | 30415 | 9 | 7 | 38 | NO | YES | NO | NO | YES | NO | -12 | -18 | 8 | 236 | 6 | 13 | 12 | 0 | 0 | 0 | YES | YES | NO | NO |
| 96 | 51 | 663707 | 9 | 6 | 54 | NO | NO | NO | YES | - | NO | -18 | -21.8 | 10 | 200 | 10 | 12 | 6 | 0 | 0 | 0 | YES | YES | NO | NO |
| 97 | 55 | 966571 | 9 | 6 | 54 | NO | N0 | NO | YES | - | NO | -19 | -23 | 10 | 200 | 10 | 12 | 6 | 0 | 0 | 0 | YES | YES | NO | NO |

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Date 21.1.2021

The Principal,
DMC, Ludhiana.

Subject: Approval of Plan of Thesis.

This is to inform you that the Faculty of Medical Sciences in its meeting held on 22.01.2021 has approved the plan of thesis of Dr Jasvinder Singh, a student of your college for DM Cardiology along with the names of Supervisor/Co-Supervisor as under:-

Topic Plan of Thesis
A prospective study for detecting cancer therapy related cardiac dysfunction in patients with breast cancer

Supervisor
Dr. Gurpreet Singh Wander
Prof. & Head,
Dept. of Cardiology,
DMCH, Ludhiana.

Co-Supervisor
Dr. Bishav Mohan
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Dr. Davinder Paul
Asst. Prof.,

The student has to submit the three copies of thesis (along with PDF format) , to the Controller of Examinations, BFUHS, Faridkot, at least six months before the commencement of theory examination, if he/she is otherwise eligible to take the examination. He /She must directed to attach a photocopy of this letter with the forwarding letter while submitting thesis to the University along with the letter of approval of University for change of supervisor/Co-Supervisor, change of topic,( if any).

Dr. S P Singh MS(Oph)
Controller of Examinations

*Note :*

3. *If any discrepancy found regarding topic of thesis or Supervisor/Co-Supervisor, inform undersigned within one month after issue of this letter.*

# A PROSPECTIVE STUDY FOR DETECTING CANCER THERPAY RELATED CARDIAC DYSFUNCTION IN PATIENTS WITH BREAST CANCER

THESIS PROPOSAL

FOR APPROVAL OF SUBJECT OF THESIS TO BE SUBMITTED

IN PARTIAL FULFILMENT OF THE REQUIREMENTS

FOR THE DEGREE OF

DOCTORATE OF MEDICINE

IN

CARDIOLOGY

OF THE

BABA FARID UNIVERSITY OF HEALTH SCIENCES
FARIDKOT

MARCH, 2020

DR JASVINDER SINGH

DEPARTMENT OF CARDIOLOGY
DAYANAND MEDICAL COLLEGE & HOSPITAL
LUDHIANA

# ABSTRACT OF PLAN OF THESIS

| | |
|---|---|
| Title | A Prospective Study For Detecting Cancer therapy related Cardiac Dysfunction In Patients With Breast Cancer |
| For the degree of | D.M Cardiology |
| Name of the candidate | Dr Jasvinder Singh |
| Supervisor | Dr Gurpreet Singh Wander, Professor & Head, Department of Cardiology, DMCH, Ludhiana |
| Co-supervisor | Dr Bishav Mohan, Professor, Department of Cardiology, DMCH, Ludhiana<br>Dr. Davinder Paul, Assistant Professor Department of Oncology, DMCH, Ludhiana |
| Institution | Dayanand Medical College & Hospital, Ludhiana |
| University | Baba Farid University of Health Sciences, Faridkot |

**Introduction**: Breast cancer is most commonly diagnosed cancer in women. Neoadjuvant chemotherapy with drugs like anthracycline, taxanes and immunotherapy have to be very effective in breast cancer. Cancer therapy related cardiac dysfunction (CTRCD) is most undesirable side of chemotherapy occurring in approx. 10 % of the patients. Present study is to evaluate the cardiovascular complications of cancer therapy used for breast cancer.

**Aim of Study**: Detecting cancer therapy related cardiac dysfunction in patients with breast cancer.

**Materials & Methods**: All newly diagnosed breast cancer patients aged more than 18 years who will be come to DMCH for chemotherapy will be enrolled. All patients will be questioned for risk factors of IHD, any h/o radiation, liver disease or cardiac disease. Body mass index and ECOG performance status of all patients will be recorded at baseline. A detailed history and examination of cardiovascular system will be done at baseline and at each follow up. Investigations like Renal function test, liver function test, 12 lead ECG, CXR, Echocardiography will be done at baseline, at mid of chemotherapy and at end of chemotherapy. MUGA will be done in patients in whom Echocardiography window will be poor.

**Clinical Significance**: In India there are very few studies reporting cardiac dysfunction in patient's receiving chemotherapy for breast cancer. The present study is planned with the aim to evaluate the incidence and timing of occurrence of cardio toxicity in Indian population.

**Keywords**: breast cancer, cardiac dysfunction, chemotherapy, anthracycline, CTRCD.

(Signature) (Signature) (Signature) (Signature) (Signature)
Candidate Co-Supervisor Co-Supervisor Supervisor Principal

# CERTIFICATE OF FACILITIES AVAILABLE

This is to certify that the facilities for work on the subject of thesis titled **"A PROSPECTIVE STUDY FOR DETECTING CANCER THERAPY RELATED CARDIAC DYSFUNCTION IN PATIENTS WITH BREAST CANCER"** exist in the Department of Cardiology, DMC&H, and Ludhiana and will be provided to the candidate. We will see that the data being included in the thesis is genuine and is collected by the candidate himself/herself under our supervision and guidance.

**Supervisor**

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Place : Ludhiana

Date : 01/05/2020

# APPROVAL PROFORMA
# BY RESEARCH & ETHICAL COMMITTEE
# DAYANAND MEDICAL COLLEGE & HOSPITAL, LUDHIANA

| | |
|---|---|
| **Name of candidate** | Dr. Jasvinder Singh |
| **Department** | Cardiology |
| **Topic of Thesis** | A PROSPECTIVE STUDY FOR DETECTING CANCER THERAPY RELATED CARDIAC DYSFUNCTION IN PATIENTS WITH BREAST CANCER |
| **Likely date of appearing in PG examination** | MAY, 2022 |
| **Date of enrollment** | |
| **Name of Head of Department** | Dr. Gurpreet Singh Wander |
| **1) Supervisor** | Dr. Gurpreet Singh Wander |
| **2) Co-Supervisor(s)** | Dr. Bishav Mohan<br>Dr. Davinder Paul |
| **Signature of Members of Research Committee with Stamp** | **Signature of Members of Ethics Committee with Stamp** |
| Dr. Jaspal Singh<br>(Professor & Head, Surgery) | Mr. A K Jindal<br>(Member, Ethics Committee) |
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| Dr. Sandeep Kaushal<br>(Assistant Dean Academics) | Dr. Deepinder K Chhina<br>(Professor & Head, Microbiology) |
| Dr. Rajoo Singh Chhina<br>(Dean Academics) | Dr. Neena Sood<br>(Professor & Head, Pathology) |
| Dr. Gurpreet S Wander<br>(Vice Principal) | Dr. Gurpreet S Wander<br>(Vice Principal) |
| | Dr. Gagandeep Singh<br>(Secretary, Ethics Committee<br>Professor & Head, Neurology) |

**Approved: Yes / ~~No~~**

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**Approved: Yes / ~~No~~**

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# BABA FARID UNIVERSITY OF HEALTH SCIENCES, FARIDKOT

## PROFORMA FOR REGISTRATION OF SUBJECT FOR DISSERTATION

| | | |
|---|---|---|
| 1 | NAME OF THE CANDIDATE AND ADDRESS | Dr. Jasvinder Singh |
| 2 | NAME OF THE INSTITUTE | DAYANAND MEDICAL COLLEGE AND HOSPITAL, LUDHIANA |
| 3 | COURSE OF STUDY AND SUBJECT | DM CARDIOLOGY |
| 4 | DATE OF ADMISSION OF COURSE | 26 August 2019 |
| 5 | TITLE OF THE TOPIC | A PROSPECTIVE STUDY FOR DETECTING CANCER THERAPY RELATED CARDIAC DYSFUNCTION IN PATIENTS WITH BREAST CANCER |

## 6 BRIEF RESUME OF THE INTENDED WORK

### 6.1 NEED FOR THE STUDY

Global cancer burden is estimated to be 18.1 million new cases and 9.6 million deaths in 2018 (GLOBOCAN 2018). One in 5 men and one in 6 women worldwide develop cancer during their lifetime and one in 8 men and one in 11 women die from the disease.[1]

Breast cancer is most commonly diagnosed cancer in women (24.2% of total cases). That means one in four of all new cases diagnosed worldwide are breast cancer. Breast cancer is most common in 154 of the 185 countries. Breast cancer is the leading cause of cancer death in women (15.0%), followed by lung cancer (13.8%) and colorectal cancer (9.5%), cervical cancer ranks fourth (7.5%).[1]

According to Globocon 2012, India along with United States and China accounts for almost one third of global breast cancer burden .Breast cancer has been ranked first among Indian females with age adjusted rate as 25.8 per 1,00,000 women and mortality 12.7 per 1,00,000 women. Age adjusted incidence rate of breast cancer was found as high as 41 per 100000 women from Delhi, followed by Chennai (37.9), Bangalore (34.4), and Thiruvananthapuram (33.7).[2]

Treatment options for breast cancer are surgery, cytotoxic chemotherapy, radiation therapy and molecular targeted endocrine therapy. At present, anthracyclines (epirubicin, doxorubicin, daunorubicin, idarubicin) and taxanes (paclitaxel) are the two major classes of drugs for breast cancer treatment. Anthracyclines are the most commonly used and effective drugs for breast cancer treatment. Doxorubicin and epirubicin are commonly used in clinical practice. Cardio toxicity of Anthracycline is a prominent risk leading to morbidity and severely impacting quality of life in the patients with breast cancer.[3]

The total cumulative dose of anthracyclines is the most significant risk factor for cardiac dysfunction. Therefore it is recommended that cumulative dose of doxorubicin should not exceed 400 mg/m$^2$, and for epirubicin 900 mg/m$^2$, for daunorubicin 800mg/m$^2$.[3] Doxorubicin is associated with a 5% incidence of congestive heart failure when the cumulative dose of

400mg/m$^2$ is reached.[4,5] The most commonly accepted pathophysiological mechanism of Anthracycline induced toxicity is the oxidative stress hypothesis, which suggest that generation of reactive oxygen species and lipid peroxidation of the cell membrane damage cardiomyocytes.

Cardio toxicity of Anthracycline may be acute, early and or late. Acute toxicity, predominately supraventricular arrhythmia, transient LV dysfunction and ECG changes develop in <1 % of the patients immediately after infusion and is usually reversible. Early effect occur within one year of the treatment, while late manifest themselves after several years (median 7 years after treatment).[6]

A recent study by Cardinal et al involving 2625 patients (mean follow up of 5.2 years) showed 9% overall incidence of cardio toxicity after Anthracycline treatment and 98% of cases occurred within first year and were asymptomatic.[7] Risk factors for Anthracycline induced toxicity include, cumulative dose, infusion regimen, preexisting cardiac condition, hypertension , concomitant chemotherapy and age >65 years.[8]

Other conventional chemotherapies can induce myocardial dysfunction and heart failure are Cyclophosmamide, Cisplatin, Ifosamide, and Taxanes (Paclitaxel and Docetaxel). In combination with or after Anthracycline also appear to increase the incidence of H F, however contribution of individual drug in multidrug regimen is difficult to assess.[9]

Immunotherapies and targeted therapies have lead to improvement in efficacy of cancer drugs. Inhibition of human epidermal growth factor receptor 2 (HER 3) signalling with either antibodies (Tratuzumab, Pertuzumab, Tratuzumab – Emtasine) have improved outcome in patients with HER2 positive breast cancer when used in conjunction with chemotherapies.[10] Based on large scale clinical trials rate of cardiac dysfunction ranged from 7 to 34%, with heart failure rates between 0- 4%. When Trastuzumab used concomitantly with Anthracyclines, rates of heart failure were 6.2% and <20.1% after one and five years respectively.[11] In patients receiving trastuzumbab, cardio toxicity is most common reason for treatment interruption in 13.5 % of the patients.[12]

Radiation exposure associated with increased risk of ischemic heart disease in patients with breast cancer. Radiation to the left breast is of

particular concern given its anatomical proximity to the heart, and studies have shown increased cardiovascular events in patients receiving left sided radiotherapy compared to right side. Marked interstitial myocardial fibrosis is common in radiation induced cardio toxicity.[13]

Cardio toxicity induced by Anthracyclines can be prevented by limiting cumulative dose, prolonged administration time (infusion over 24 – 96 hours), strengthening the monitoring of cardio toxicity and use of liposomal Anthracycline. Non pharmacological measures should be promoted which include healthy diet, smoking cessation, regular exercise and weight control. Patients presenting with heart failure should be treated with guidelines of heart failure.

In India there are very few studies reporting cardiac dysfunction in patient's receiving chemotherapy for breast cancer. The present study is planned with the aim to evaluate the incidence and timing of occurrence of cardio toxicity in Indian population.

## 6.2 REVIEW OF LITERATURE

In 2019, Devender Kodati et al, conducted retrospective study on adverse effects of chemotherapy in breast cancer in Telengana, India. **353 patients** were enrolled. During chemotherapy, some patients were given AC, T **(doxorubicin, cyclophosmamide, paclitaxel)** regimen and few patients were given CAF (cyclophosmamide, doxorubicin and 5FU regimen. Among 353 patients, 344 patients shown adverse effects and 9 patients were without any adverse effects. They have identified 1,157 adverse effects in total of 344 patients, among them **16.5%** were found to be cardiac effects, 60.5% were haematological effects and 22.6% were found to be in USG abdomen.[14]

In **2017,** a study was conducted by Mohammad Osman et al, in which they evaluated the effect of **Paclitaxel** on cardiac ejection fraction at Egypt. A total of **50 subjects** were enrolled between 2011 to 2015 and follow up done till **30 months**. During 30 months follow up **10 (20%)** patients developed grade 1 (up to 5 % decrease in EF from baseline) and 2 (asymptomatic decline in EF of > 5% but < 20% from baseline) cardio toxicities. Paclitaxel cardio toxicity increased among patients with high risk features including diabetes mellitus, hypertension, prior radiotherapy to chest wall, performance status 2(ECOG) and age > 60 years.[15]

In 2015, Daniel Cardinale et al conducted a study on early detection of **Anthracycline** cardio toxicity and improvement with heart failure treatment at Milan, Italy. The LVEF was assessed at baseline, every 3 months during chemotherapy and for the following year, every 6 months over the following 4 years, and yearly afterward in heterogeneous cohort of **2625 patients** receiving Anthracycline containing therapy. Recovery was from cardio toxicity was defined as partial (LVEF increase > 5 absolute points and > 50%) or full (LVEF increase to baseline value). The median follow was up of **5.2 years**. The overall incidence of cardio toxicity was **9% (n=226).** The median time elapsed between end of chemotherapy and cardio toxicity development was 3.5 months. In 98% of cases cardio toxicity occurred within first year. 11% (n=25) patients had full recovery and 71% (n=160) patients have partial recovery.[7]

In 2009, study was conducted by Anil Grover et al, on the **Doxorubicin** induced cardio toxicity in adult patients on chemotherapy in Mumbi, India.

Study was done between January 2000 to June 2001. ECG, CXR and echocardiography was done at baseline, at 300mg/$m^2$ and at 450 mg/$m^2$ cumulative doses of Doxorubicin. **30 patients** were enrolled. **One (3%)** patient developed congestive heart failure, while 8 (27%) patients developed subclinical cardiac dysfunction. Concomitant use of cyclophosmamide significantly increase the risk of cardiac dysfunction (P=0.048), while low BMI (<20 kg/$m^2$) and pre-existing cardiac disease showed trend towards increased risk of cardiac dysfunction (p=0.07 for both).[16]

In 2008, Marianne Ryberg et al, conducted a study on new insight into epirubicin cardiac toxicity. **1097** patients of breast cancer treated with Anthracycline were enrolled. A total of **11.4%** of patients developed cardio toxicity. Risk factors for cardio toxicity included increased cumulative dose of epirubicin, patient age, and predisposition of cardiac disease, h/o mediastinal irradiation, or antihormonal treatment for metastatic disease.[17]

In 2006, P. Fumoleau et al, conducted a study on long term toxicity after adjuvant epirubicin based chemotherapy in early breast cancer. French adjuvant study group results. **3577** patients were analysed retrospectively, 2553 received epirubicin, 662 received hormonotherapy alone and 362 had no systemic treatment. After **7 year** of median follow up the risk of developing a LVD after epirubicin based adjuvant chemotherapy was **1.36% and 0.21%** in non epirubicin exposed group.[18]

## 6.3 AIMS AND OBJECTIVES OF THE STUDY

- To evaluate baseline clinical profile and echocardiography findings in patients with Breast cancer.
- To assess the cardiovascular complications of cancer therapy in patients with breast cancer with special emphasis on cancer therapy related cardiac dysfunction.

## 7.0 MATERIALS AND METHODS

### 7.1 SOURCE OF DATA:

All newly diagnosed breast cancer patients aged more than 18 years who will be come to DMCH for chemotherapy from 1st march 2020 onwards will be enrolled and follow up will be done.

### 7.2 METHOD OF COLLECTION OF DATA

**Inclusion Criteria:**

1. Patients who have histologically proven breast cancer.
2. Age more than 18 years.

**Exclusion Criteria:**

1. Patients less than 18 years.
2. Pregnant and lactating women.
3. Past history of Valvular Heart Disease, Cardiomyopathy, CHF, Ischemic Heart Disease, symptomatic arrhythmia.

All patients will be questioned for risk factors of IHD, any h/o radiation, liver disease or cardiac disease. Body mass index and ECOG performance status of all patients will be recorded at baseline. A detailed history and examination of cardiovascular system will be done at baseline and at each follow up. Investigations like Renal function test, liver function test, 12 lead ECG, CXR, Echocardiography will be done at baseline, at mid of chemotherapy and at end of chemotherapy. MUGA will be done in patients in whom Echocardiography window will be poor.

During echocardiography, fractional shortening, ejection fraction, global longitudinal and circumferential shortening will be evaluated, beside other routine parameters. In order to reduce inter-observer variability, echocardiography will be performed by same physician for each patient at different times of pints. All patients included in the study will have left ventricular ejection fraction greater than 50 % at baseline.

Cardio toxicity will be divided into acute (within one week), early (one week to one year) and late onset (after one year).

Cardio toxicity will be defines as a decrease in LVEF > 10 percentage points from the baseline or < 50 %; global longitudinal strain (GLS) > 15 %

relative percentage reduction from the baseline. On Nuclear Cardiac Imaging (MUGA) scan >10 percentage points decrease in LVEF or < 50 %.[19]

Classification for cardiac toxicity and heart failure:

(CTCAE[19], version 4.03: Common terminology criteria for adverse effects.)

| Classification | Grade 1 | Grade 2 | Grade 3 | Grade 4 |
|---|---|---|---|---|
| CTCAE Heart Failure | Asymptomatic with lab (BNP) or cardiac imaging abnormalities | Resting EF= 50%- 40%, 10 % to 19% drop from baseline | Resting EF= 39%- 20%, > 20 % drop from baseline | Resting EF = < 20 % |
| NYHA classification | Grade 1 , no limitation of activity | | Grade II, mild limitation of activity Grade III, Marked limitation of activity. | Grade IV, confined to bed or chair. |

This study is approved by ethical committee of the institute and all patients will be enrolled after informed consent.

**Study Design:** A prospective study will be conducted at Dayanand Medical College, Ludhiana, between March 1, 2020 to March 31, 2021.

**OUTCOME:** All the patients receiving chemotherapy should be screened for cardiac toxicity. Early detection and treatment can improve morbidity and mortality of the patients. At present limited cardio protective strategies are available. There is no prophylaxis available. New strategies are required to help combat cardio toxicity derived from Anthracycline and other chemotherapy. Personalized medicine and targeted chemotherapy may helpful in reducing cardio toxicity.

**STATISTICAL ANALYSIS:** Data will be described in terms of range; mean ±standard deviation (± SD), median, frequencies (number of cases) and relative frequencies (percentages) as appropriate. Comparison of quantitative variables will be done using Paired t-test. A probability value (p value)less than 0.05 will be considered statistically significant. All statistical calculations will be done using SPSS (Statistical Package for the Social Science) SPSS 21 version statistical program for Microsoft Windows.

**7.3 DOES THE STUDY REQUIRE ANY INVESTIGATIONS OR INTERVENTIONS TO BE CONDUCTED ON PATIENTS OR OTHER HUMANS OR ANIMALS? IF SO, PLEASE DESCRIBE BRIEFLY.**

NO

**7.4 HAS ETHICAL CLEARENCE BEEN OBTAINED FROM YOUR INSTITUTION IN CASE OF 7.3?**

ATTACHED HEREWITH

## 8.0 LIST OF REFERENCES


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# PROFORMA

Enrolment date: ---------- Sr. No. ----------

Name: ---------- Age: ----------

Adm No. : ---------- Address: ----------

Occupation: ---------- phone no. ----------

Diagnosis: ---------- Stage: ----------

P/H/O of RT/CT/Surgery ----------

Type of Chemotherapy: ----------

ECOG performance status: ----------

Physical Examination:

Height: ---------- BSA: ----------

Weight: ---------- BMI: ----------

Systolic BP: ---------- Diastolic BP: ----------

Pallor: ------ Icterus: ---------- Cyanosis: -------- Edema: ---------

JVP: -------- Ascites: ---------- LAP: ----------

Signature of Candidate

Signature of Supervisor

**CVS Examination:** ----------

| | Positive findings | |
|---|---|---|
| Inspection | | |
| Palpation | | |
| Auscultation | Aortic area | Pulmonary area |
| | Mitral area | Tricuspid area |

**Cardiovascular risk Factors:**

| | |
|---|---|
| Diabetes Mellitus | |
| Hypertension | |
| Smoking | |
| CAD | |
| Obesity | |
| Sedentary life style (MET) | |
| Family h/o CAD | |

**Past History Of:**

| | |
|---|---|
| Valvular Heart Disease | |
| Cardiomyopathy | |
| Ischemic Heart Disease | |
| Arrhythmia | |
| Congestive heart failure | |



Signature of Candidate

Signature of Supervisor

**Base line investigation:**

| | Before chemotherapy | Mid of the chemotherapy | End of the chemotherapy |
|---|---|---|---|
| Chemotherapy and dose | | | |
| Radiotherapy | | | |
| Physical examination | | | |
| NYHA class | | | |
| Systolic BP (mm of Hg) | | | |
| Diastolic BP (mm of Hg) | | | |
| Hemoglobin (g/dl) | | | |
| TLC (per $mm^{3)}$ | | | |
| Platelet (per $mm^{3)}$ | | | |
| RBS (mg/dl) | | | |
| Total Cholesterol (mg/dl) | | | |
| Bilirubin (mg/dl) | | | |
| SGOT (IU/L) | | | |
| SGPT (IU/L) | | | |
| Total protein ( g/dl) | | | |
| Albumin (g/dl) | | | |
| Blood Urea (mg/dl) | | | |
| S creatinine (mg/dl) | | | |
| CXR | | | |
| ECG Changes | | | |

Signature of Candidate

Signature of Supervisor

**ECHOCARDIOGRAPHY**

| | Before chemotherapy | Mid of the chemotherapy | End of the chemotherapy |
|---|---|---|---|
| Aorta root (mm) | | | |
| LA SIZE (s) (mm) | | | |
| LA SIZE (d) (mm) | | | |
| LAVI (s) | | | |
| LAVI (d) | | | |
| LVEDV | | | |
| LVMPI | | | |
| CRS | | | |
| Global Circumferential strain (%) | | | |
| Global longitudinal strain (%) | | | |
| MAPSE | | | |
| PASP | | | |
| E/A | | | |
| E/e' | | | |
| S' | | | |
| e' | | | |
| a' | | | |
| Ejection fraction (%) | | | |
| Global longitudinal strain (%) | | | |
| Longitudinal Strain rate | | | |
| MR (mild/mod/severe) | | | |
| AR (mild/mod/severe) | | | |
| TR (mild/mod/severe) | | | |
| PR (mild/mod/severe) | | | |
| Pericardial effusion | | | |



Signature of Candidate

Signature of Supervisor

**MUGA scan:** ----------

**EASTERN COOPERATIVE ONCOLOGY GROUP (ECOG)** performance status:

| GRADE | PERFORMANCE STATUS |
|---|---|
| 0 | Fully active, able to carry on all pre disease performance without restriction. |
| 1 | Restricted in physical strenuous activity but ambulatory and able to carry out work of a light or sedentary nature e.g. light house hold work, office work. |
| 2 | Ambulatory and capable of all self-care but unable to carry out any work activities; up and about more than 50 % of waking hours. |
| 3 | Capable of only limited self-care; confined to bed or chair more than 50 % of waking hours. |
| 4 | Completely disabled; cannot carry on any self-care; totally confined to bed or chair. |
| 5 | Dead |

Signature of Candidate

Signature of Supervisor

CTRCD: Cancer related cardiac dysfunction

DNA: Deoxyribonucleic acid

LV: left ventricle

CVD: cardio vascular disease

CHF: congestive heart failure

ECOG: eastern cooperative oncology group

LVEF: left ventricle ejection fraction

GLS: global longitudinal strain

IHD: ischemic heart disease

MUGA: multigated acquisition scan

EF: ejection fraction



Signature of Candidate

Signature of Supervisor

## INFORMED PATIENT CONSENT

Date: _____

I.....D/o, W/o, S/o.....
.....am willing to participate in the study **"A PROSPECTIVE STUDY FOR DETECTING CANCER THERAPY RELATED CARDIAC DYSFUNCTION IN PATIENTS WITH BREAST CANCER"** The procedure with its complications has been explained to me in local vernacular language. I have fully understood that no special tests and extra expenditure in any form, merely for the purpose of thesis is being carried out. I am free to opt out the study any time without assigning any reason.

.....
Signature of the Witness

.....
Signature of the patient

Name:

**Signature of Candidate**

**Signature of Supervisor**

# मरीज अनुमति फार्म

तिथि _____

मैं _____ पत्नी/पुत्र/पुत्री _____

निवासी _____

इस शोधकार्य **"A PROSPECTIVE STUDY FOR DETECTING CANCER THERAPY RELATED CARDIAC DYSFUNCTION IN PATIENTS WITH BREAST CANCER"** में भाग लेने के लिए सहमत हूँ। मैं इस शोधकार्य में भाग लेने के लिए अपनी स्वेच्छा से तैयार हूँ। मैं पुष्टि करता/करती हूँ की यह स्वीकृति देने के लिए मुझे कोई आर्थिक प्रलोभन नहीं दिया गया और न ही दबाव डाला गया है। मुझे इस शोधकार्य का उद्देश्य स्पष्ट कर दिया गया है और मुझे यह विश्वास है की यह विज्ञान और मानवता के लाभ के लिए है। मुझे इस शोधकार्य में होने वाले जोखिम के बारे में समझा दिया गया है और मेरी समझ में यह जोखिम बहुत मामुली है।

मैं इस शोधकार्य में भाग लेने के सम्बन्ध में किसी भी समय अपनी अस्वीकृति व्यक्त कर सकता/सकती हूँ और मेरे अस्वीकृति व्यक्त करने का मेरे इलाज पर कोई प्रभाव नहीं पड़ेगा।

_____ _____

गवाह के हस्ताक्षर रोगी के हस्ताक्षर/अंगूठे का निशान

नाम: नाम:

_____

अन्वेषक के हस्ताक्षर

_____

विद्यार्थी के हस्ताक्षर

# ਮਰੀਜ਼ ਰਜ਼ਾਮੰਦੀ ਫਾਰਮ

ਮਿਤੀ_____

ਮੈ_____ਪਤਨੀ/ਪੁੱਤਰ/ਪੁੱਤਰੀ_____

ਵਾਸੀ _____

**"A PROSPECTIVE STUDY FOR DETECTING CANCER THERAPY RELATED CARDIAC DYSFUNCTION IN PATIENTS WITH BREAST CANCER"** ਤੇ ਚਲ ਰਹੀ ਖੋਜ ਵਿਚ ਹਿੱਸਾ ਲੈਣ ਲਈ ਰਜ਼ਾਮੰਦ ਹਾਂ। ਇਸ ਖੋਜ ਕੰਮ ਵਿਚ ਹਿੱਸਾ ਲੈਣ ਲਈ ਮੈ ਆਪਣੀ ਮਰਜ਼ੀ ਨਾਲ ਤਿਆਰ ਹਾਂ। ਮੈ ਇਹ ਦਸਣਾ ਚਾਹੁੰਦਾ ਹਾਂ/ ਚਾਹੁੰਦੀ ਹਾਂ ਕੇ ਇਹ ਰਜ਼ਾਮੰਦੀ ਦੇਣ ਵਾਸਤੇ ਮੈਨੂ ਕਿਸੇ ਵੀ ਤਰਾਂ ਦਾ ਲੋਭ-ਲਾਲਚ ਨਹੀ ਦਿੱਤਾ ਗਿਆ ਅਤੇ ਨਾ ਹੀ ਕੋਈ ਦਬਾ ਪਾਇਆ ਗਿਆ ਹੈ। ਮੈਨੂ ਇਸ ਖੋਜ ਦਾ ਮਨੋਰਥ ਸਮਝਾ ਦਿੱਤਾ ਗਿਆ ਹੈ ਅਤੇ ਮੈਨੂ ਇਹ ਭਰੋਸਾ ਦਵਾਇਆ ਗਿਆ ਹੈ ਕੇ ਇਹ ਖੋਜ ਵਿਗਿਆਨ ਅਤੇ ਮਾਨਵਤਾ ਦੀ ਭਲਾਈ ਲਈ ਹੈ। ਮੈਨੂ ਇਸ ਖੋਜ ਵਿਚ ਹੋਣ ਵਾਲੇ ਖਤਰੇ ਬਾਰੇ ਸਮਝਾ ਦਿੱਤਾ ਗਿਆ ਹੈ ਅਤੇ ਮੈਨੂ ਇਹ ਯਕੀਨ ਹੈ ਕੇ ਇਹ ਖਤਰਾ ਬਹੁਤ ਮਾਮੂਲੀ ਹੈ। ਮੈਨੂ ਇਸ ਖੋਜ ਕੰਮ ਵਿਚ ਹਿੱਸਾ ਲੈਣ ਦਾ ਢੰਗ – ਤਰੀਕਾ ਸਮਝਾ ਦਿੱਤਾ ਗਿਆ ਹੈ।

ਮੈ ਇਸ ਖੋਜ ਕੰਮ ਵਿਚ ਹਿੱਸਾ ਲੈਣ ਬਾਰੇ ਆਪਣੀ ਰਜ਼ਾਮੰਦੀ ਕਿਸੇ ਵੀ ਸਮੇ ਵਾਪਸ ਲੈ ਸਕਦਾ ਹਾਂ/ ਸਕਦੀ ਹਾਂ ਅਤੇ ਮੇਰੀ ਰਜ਼ਾਮੰਦੀ ਵਾਪਸ ਲੈਣ ਦਾ ਮੇਰੇ ਇਲਾਜ ਤੇ ਕੋਈ ਅਸਰ ਨਹੀ ਹੋਵੇਗਾ।

_____ _____

ਗਵਾਹ ਦੇ ਹਸਤਾਖਰ ਮਰੀਜ਼ ਦੇ ਹਸਤਾਖਰ

ਮਿਤੀ_____ ਮਿਤੀ_____

ਪਤਾ _____ ਪਤਾ _____

_____

ਨਿਰੀਖਕ ਦੇ ਹਸਤਾਖਰ

_____

ਸਿਖਿਆਰਥੀ ਦੇ ਹਸਤਾਖਰ